The BULLETIN

American Society of Hospital Pharmacists

OFFICIAL PUBLICATION OF THE AMERICAN SOCIETY OF HOSPITAL PHARMACISTS

DON E. FRANCKE, Editor

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American Society of Hospital Pharmacists

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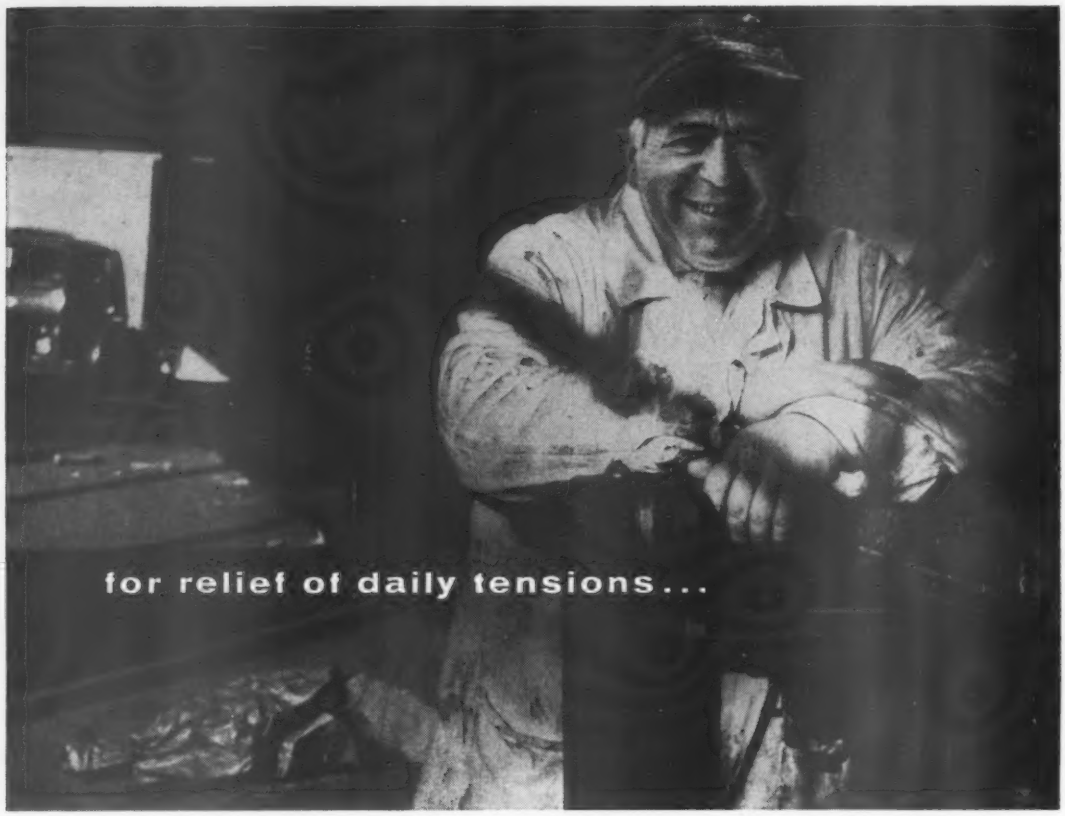

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Ectylurea, AMES
(higher melting isomer of
2-ethylcrotonylurea)

the power of gentleness

helps patients face everyday anxieties and tensions

*"...mild action promotes an over-all calmness..."**

New and Different • not a hypnotic-sedative—unrelated to any available chemo-psychotherapeutic agent • no evidence of cumulation or habituation • does not cause gastric hyperacidity • unusually wide margin of safety—no significant side effects

Dosage: 150-300 mg. three or four times daily.

Supplied: 300 mg. scored tablets, bottles of 48.

*Ferguson, J. T.: J. Am. Geriatrics Soc. *4*:1080, 1956.

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DRUG EVALUATIONS

by the Council on Pharmacy and Chemistry of the American Medical Association

The following monographs and supplemental statements on drugs have been authorized by the Council on Pharmacy and Chemistry of the American Medical Association for publication and inclusion in *New and Nonofficial Remedies*. They are based upon the evaluation of available scientific data and reports of investigations. In order to make the material even more valuable, dosage forms and preparations of individual drugs have been added to the monographs. These dosage forms and preparations were not taken from material published in the *Journal of the American Medical Association* by the Council on Pharmacy and Chemistry; rather, they were obtained from such manufacturers' brochures, news releases, etc., which were available to us at the time of publication. An attempt has been made to make the list of dosage forms as complete as possible. However, no guarantee can be made that the list of preparations is complete and it is suggested that hospital pharmacists consult manufacturers' releases for additional dosage forms and preparations.

The issues of the *Journal of the American Medical Association* from which each monograph has been taken is noted under each monograph. Monographs in this issue of THE BULLETIN include those published in the *Journal* to December, 1956.

NOTICE

New and Nonofficial Remedies 1957 is now available from your local bookstore and from the publishers, J. B. Lippincott Company, Philadelphia, Pa. This 1957 edition contains monographs of drugs evaluated by the Council on Pharmacy and Chemistry of the American Medical Association and published in the Journal of the A.M.A. to October 1956. This issue of THE BULLETIN contains those drugs evaluated and published during October and November 1956.

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Notice Of Change In Operation

Listing Of Trade Names Extended

The Council has extended its current policy of listing known commercial names for preparations of individual drugs with published monographs (*J.A.M.A. 160*:50 [Jan. 7] 1956) so as to provide for their parenthetic inclusion in supplemental statements on additional uses of previously evaluated drugs, which also are published in the New and Nonofficial Remedies section of the Council's column in THE JOURNAL. The Council also has altered its former policy respecting special reports on drugs and drug therapy not intended for inclusion in N.N.R. to provide for parenthetic insertion of commercial names in such reports when the nonproprietary terminology for drugs that are mentioned is not considered to be generally well known.

The Council will continue to list known commercial names at the end of N.N.R. monographs but will follow the parenthetic method for their insertion after the initial appearance of nonproprietary terminology in the texts of N.N.R. supplemental statements and, when considered necessary for ready identification, in Council reports. The changes involved will be implemented in subsequent issues of THE JOURNAL and annual editions of New and Nonofficial Remedies. The Council hopes this extension of policy for listing trade names will further aid physicians in the identification of drugs that the Council regularly describes under nonproprietary terminology. Trade names are listed as a matter of information, and the Council assumes no responsibility for either their suitability or the quality of preparations to which they are applicable.

As in the past, manufacturers and distributors are invited to inform the Council of commercial names applied in the United States of preparations of drugs.

J. Am. Med. Assoc. 162:974 (Nov. 8) 1956.

Bethanechol Chloride

Use for Paralytic Ileus and Urinary Retention After Ganglionic Blockade

The Council has evaluated the additional use of the parasympathomimetic (cholinergic) agent bethanechol chloride for the treatment of paralytic ileus and urinary retention caused by the parasympatholytic action of certain ganglionic blocking agents used in the treatment of hypertension. These complications can result from hypersensitivity to the drugs, over-dosage, or, in the case of ileus, inadequate dietary and/or laxative management. Bethanechol previously has been described as useful for the treatment of postoperative abdominal distention and paralytic ileus, and also for neurogenic atony of the urinary bladder with retention. On the basis of currently available information, the Council further

concluded that it is helpful in aborting or relieving intestinal stasis and urinary retention caused by ganglionic blockade. The blocking agents against which it is useful include the salts of hexamethonium and mecamylamine hydrochloride. Whenever possible, cholinergic therapy with bethanechol chloride should be initiated before the appearance of acute symptoms.

For these indications, bethanechol chloride may be administered orally, sublingually, or subcutaneously (never intramuscularly or intravenously), the oral or sublingual route being preferred unless symptoms are unusually severe. Dosage must be individualized according to severity of symptoms and degree of response. The administration of 10 mg. orally or sublingually three times daily appears to be the most commonly employed dosage. The usual subcutaneous dose is 5 mg.; however, since some patients may experience side-effects and respond to as little as 2.5 mg., the latter should be used as an initial parenteral dose and the minimum effective dose determined for each patient by observing the response to injections at intervals of 15 to 30 minutes.

The Council voted to amend New and Nonofficial Remedies to describe this additional use of bethanechol chloride.

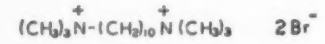
Merck Sharp & Dohme, Division of Merck & Co., Inc., cooperated by furnishing scientific data to aid in the evaluation of the use of bethanechol chloride for paralytic ileus and urinary retention after ganglionic blockade.

J. Am. Med. Assoc. **162**:731 (Oct. 20) 1956.

Decamethonium Bromide

Syncurine® Bromide

DECAMETHONIUM BROMIDE is decamethylenebis (trimethylammonium bromide).—The structural formula of decamethonium bromide may be represented as follows:



Actions and Uses

Decamethonium bromide, a synthetic quaternary ammonium compound, is a potent skeletal muscle relaxant. Like tubocurarine, it blocks motor impulses at the myoneural junction but is about three times as potent in this respect as equal amounts of tubocurarine. After intravenous administration, muscle relaxation becomes apparent within 1 minute and is maximal at 3 to 4 minutes. Muscle activity begins to return after 8 to 10 minutes and has usually returned to normal after 20 to 30 minutes. Thus, the duration of action of decamethonium is intermediate between that of tubocurarine and succinylcholine, being more fleeting than that of the former but more persistent than that of the latter. Unlike tubocurarine, the drug does not produce histamine-like effects (bronchospasm and laryngospasm), nor does it cause ganglionic blockade. Any effects on pulse and blood pressure are not due to decamethonium per se but develop secondarily as a result of inadequate ventilation during respiratory depression or apnea. Decamethonium does not potentiate or act synergistically with ether or any of the commonly employed anesthetic agents. No cumulative effects are noted after repeated administration; on the contrary, tachyphylaxis (decreased effectiveness with repeated administration of the same dose) has been observed.

Decamethonium bromide effectively produces muscle relaxation during surgical procedures carried out with the patient under general anesthesia. The drug also is useful for facilitating endotracheal intubation or as an adjunct in electroconvulsive therapy.

Respiratory depression, which can occur after the administration of all myoneural blocking agents, is also a potential danger with decamethonium, especially in the deeper planes of anesthesia. Current evidence indicates that both the morbidity and mortality associated with the use of decamethonium and tubocurarine are identical. The anticholinesterases and edrophonium chloride are of no value as antagonists to overdosage; therefore, it is essential that facilities for controlled respiration and oxygen administration be immediately available when the drug is used.

Dosage

Decamethonium bromide is administered by single intravenous injection, which may be repeated as necessary. Since the drug is miscible with thiopental sodium, it is sometimes administered in combination with this agent for the induction of anesthesia. The response to decamethonium varies greatly from patient to patient. Doses that are suboptimal for some may cause respiratory depression in others; therefore, dosage must be individually determined. The usual dose varies from 0.5 to 3 mg., depending on the individual response and the degree of relaxation desired. The response to the drug is quite reproducible in a given patient from day to day.

Preparations for use as stated for the foregoing drug are marketed under the following name: Syncurine.

Burroughs Wellcome & Co., Inc., cooperated by furnishing scientific data to aid in the evaluation of decamethonium bromide.

J. Am. Med. Assoc. **162**:731 (Oct. 20) 1956.

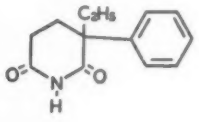
Preparations

Injection Decamethonium (Syncurine) Bromide 1 mg. per ml.; 10 ml. vials.

Glutethimide

Doriden®

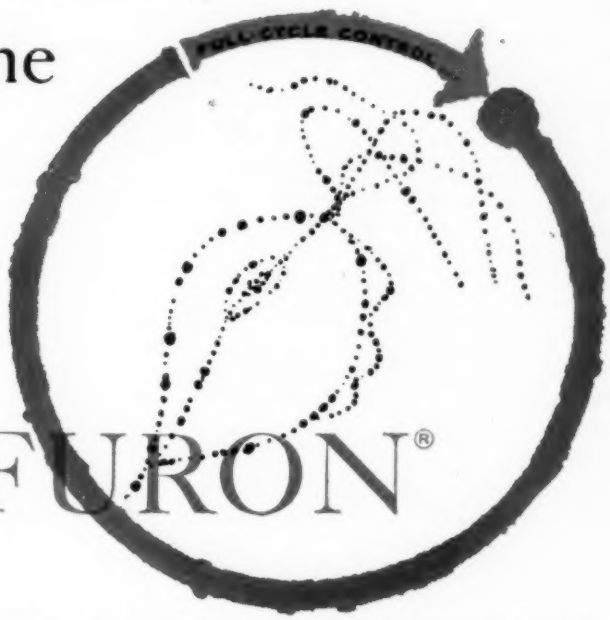
GLUTETHIMIDE is 2-ethyl-2-phenylglutarimide.—The structural formula of glutethimide may be represented as follows:



Actions and Uses

Glutethimide, a central nervous system depressant, is used as a hypnotic and sedative. It produces alterations in the electroencephalographic pattern similar to those observed after administration of chloral hydrate or barbiturates. The onset of action begins about half an hour after administration of hypnotic doses and generally lasts from 4 to 8 hours. Thus, the drug is similar in onset and duration of action to the short-acting barbiturates such as pentobarbital sodium. Little is known about its metabolic fate.

Even stubborn trichomoniasis yields... because Tricofuron is effective during menstruation, the critical time for therapy.



TRICOFURON®

Recurrences of trichomoniasis "are most likely to follow the menstrual period."[1]

"Over and over again today patients are seen with what is said to be an intractable, treatment-resistant Trichomonas infestation, but history-taking often reveals that such patients have never had treatment prescribed during any menstrual period."[2]

Menstrual blood in the vagina "forms an excellent medium for the rapid multiplication of T. vaginalis"[3] and "lowers the acidity of the vagina and hence there is a tendency to recrudescence [of trichomoniasis] at that time."[4]

Tricofuron is powerfully trichomonacidal "even in the presence of vaginal debris and menstrual blood."[3]

For 44 of 48 patients: lasting cure was obtained with a single course of Tricofuron therapy.[3]

Vaginal Suppositories—for home use—each morning and night through one cycle, including the important menstrual days. Contain 0.25% Furoxone® (brand of furazolidone) in a water-miscible base. Box of 12, each sealed in green foil.

Vaginal Powder—for office use—applied by the physician at least once a week, except during menstruation. Contains 0.1% Furoxone in an acidic powder base of lactose, dextrose, citric acid and a silicate. Bottle of 30 Gm.

References: 1. Bernstine, J. B., and Rakoff, A. E.: Vaginal Infections, Infestations and Discharges, New York, The Blakiston Company, Inc., 1953, p. 235. 2. Overstreet, E. W.: Arizona M. 10:383, 1953. 3. Schwartz, J.: Obst. Gyn., N. Y. 7:312, 1956. 4. Crossen, R. J.: Diseases of Women, St. Louis, The C. V. Mosby Company, 1953, p. 292.

EATON LABORATORIES *NORWICH, NEW YORK*

Nitrofurans—a new class of antimicrobials—neither antibiotics nor sulfonamides

Glutethimide is reported to be useful for the induction of sleep in patients with simple and nervous insomnia. Since it is short-acting, it may also be administered to patients who waken during the night. In general, the incidence of hangover is low; however, if the drug is administered during the night, some residual depression may persist. It is not effective alone as a hypnotic in the presence of pain or in patients who are extremely disturbed. On the basis of currently available evidence, it would appear that glutethimide is about as effective a hypnotic as the usually employed short-acting barbiturates but that it possesses no particular advantage over the latter except in patients who cannot tolerate barbituric acid derivatives.

Glutethimide also has been employed as a preoperative sedative and as a daytime sedative in patients with anxiety-tension states. The evidence available to date, however, is not sufficient to permit a definite conclusion regarding its ultimate usefulness for these purposes.

After administration of therapeutic doses, the principal side-effects reported to date have included skin rash, infrequently, and nausea; the latter condition is usually not severe enough to necessitate discontinuation of medication. Acute toxic effects resulting from accidental or deliberate overdosage are similar to those of all hypnotic drugs, and treatment of such intoxication should follow the same general scheme as for barbiturate poisoning. It is not known whether the drug possesses addicting potentialities, but, on the basis of present knowledge, this appears unlikely. Nevertheless, in the absence of sufficient evidence on the effects of repeated use of glutethimide in man or experimental animals, its long-term clinical use should be approached cautiously.

Dosage

Glutethimide is administered orally. The usual hypnotic dose for adults is 0.5 gm. at bedtime. This may be repeated once during the night but not less than 4 hours before arising. For daytime sedation, doses of 0.25 gm. three times daily, after meals, have been employed. Doses of 0.5 gm, the night before surgery and 0.5 to 1 gm. one hour before anesthetization have been used for preoperative sedation. Dosage for children for all indications is reduced proportionately.

Applicable commercial name: Doriden.
Ciba Pharmaceutical Products, Inc., cooperated by furnishing scientific data to aid in the evaluation of glutethimide.

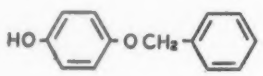
J. Am. Med. Assoc. **162**:975 (Nov. 3) 1956.

Preparations

Tablets Glutethimide (Doriden) 0.125 Gm., 0.25 Gm., and 0.5 Gm., scored.

Monobenzone Benoquin®

MONOBENZONE is *p*-benzyloxyphenol.—Monobenzyl ether of hydroquinone.—The structural formula of monobenzone may be represented as follows:



Actions and Uses

Monobenzone is a melanin-pigment-inhibiting agent. The depigmenting action of the agent was discovered accidentally when it was observed that the hands of certain workers who used rubber gloves in which it was incorporated as an antioxidant developed areas of hypopigmentation. Monobenzone produces this effect by interfering with the formation of the pigment melanin. It is believed that the drug inhibits the enzyme tyrosinase, thus blocking the oxidation of tyrosine to dihydroxyphenylalanine, a precursor of melanin. It does not destroy or inhibit melanocytes; therefore, depigmentation is temporary and reversible.

Monobenzone has been used for the treatment of various conditions that produce hyperpigmentation caused by formation of melanin. These include generalized lentigo, severe freckling, hyperpigmentation due to photosensitization, and the melasma (chloasma) of pregnancy and adrenocortical hypofunction (Addison's disease). In certain patients with these conditions, the drug may be expected to produce a gradual decrease in skin pigmentation. Successful treatment apparently depends on several factors, such as frequency of application, concentration of the drug, and individual variation in susceptibility. Not all patients experience equally satisfactory cosmetic results; some are completely resistant to the agent. Since the action of the drug depends on the inhibition of new melanin formation, it follows that depigmentation of the skin will not become apparent until the preformed pigment has been exhausted. The speed with which this is accomplished is variable; generally periods of several weeks or months are required. Since exposure to the ultraviolet rays of sunlight accelerates melanin formation under any circumstances, it is advisable to avoid excessive exposure to the sun or to employ one of the topical sun-shading agents when using monobenzone. Depigmentation usually persists for a considerable period after cessation of therapy; however, the drug does not permanently eradicate or cure hyperpigmentation. Thus, modified therapy must be continued indefinitely for continued cosmetic results. The agent is not indicated for mild to moderate freckling, since these lesions are usually seasonal and will fade spontaneously during the winter months. It has not proved of value in the treatment of *café au lait* spots, pigmented nevi, or melanoma.

Dermal irritation occurs in a substantial percentage of patients using this drug. This can range in severity from mild erythema to dermatitis. In some patients, this irritant effect is temporary and does not necessitate discontinuation of therapy; in others, an eczematous sensitization to the drug can occur. Although this is not so frequent as simple irritation, physicians prescribing this agent should warn patients about the possible occurrence of skin manifestations. The drug can also produce an excessive, and unsightly, loss of pigmentation in some patients or a patchy, uneven area of depigmentation that may extend beyond the areas desired. There is no evidence of systemic toxic effects from its external use. Although monobenzone appears to be promising as a skin depigmenting agent, further study is necessary to determine its ultimate usefulness and safety.

Dosage

Monobenzone is applied topically to the skin as a 20 percent ointment or a 5 percent lotion. The latter

IN INTRAVENOUS ANESTHESIA

Neraval
SODIUM

"... the shortest-acting thiobarbiturate so far known to us ..."[1]

- **Shorter duration of effect**[1]
- **More rapid, complete recovery**[3,5-7]
- **Diminished cumulative action**[2-4,6,8]

HOW YOUR PATIENT BENEFITS

- Rapid, pleasant recovery.
- Unusual freedom from prolonged postanesthetic depression or "hangover."
- Shortened period of postoperative incapacity.
- Heightened patient morale.

HOW YOUR HOSPITAL BENEFITS

- Less-crowded recovery rooms.
- Shortened postoperative recovery period permits earlier assignment of nurses to other hospital duties.[1]

PACKAGING

NERAVAL Sodium Sterile Powder: vials of 1 Gm. and 2 Gm., boxes of 6 and 25; vials of 5 Gm., boxes of 1 and 25.

BIBLIOGRAPHY

(1) Boone, J.D.; Munoz, R., and Dillon, J.B.: Anesthesiology *17*:284, 1956. (2) Zima, O.; von Werder, F., and Hotovy, R.: Anaesthesist *3*:244, 1954. (3) Fitzpatrick, L.J.; Clarie, D'A., and Mersch, M.A.: To be published. (4) Blake, M.W., and Perlman, P.L.: J. Pharmacol. & Exper. Therap. *117*:287, 1956. (5) Ayd, F.J., Jr.: Neraval: A new anesthetic for electroconvulsive therapy, Paper presented at annual meeting, Electroshock Research Association, Chicago, Illinois, April 29th, 1956. (6) Irwin, S.; Stagg, R.D.; Dunbar, E., and Govier, W.M.: J. Pharmacol. & Exper. Therap. *116*:317, 1956. (7) Reifferscheid, M., and Dietmann, K.: Deutsche med. Wchnschr. *79*:638, 1954. (8) Dietmann, K.: Deutsche med. Wchnschr. *79*:1748, 1954.

NERAVAL® Sodium, brand of methitural sodium.

Schering

NE-J-5116

preparation is intended for patients who have evidenced dermal intolerance to the more concentrated ointment. Experienced dermatologists indicate that the incidence of skin reactions can be further reduced if the 20 percent ointment is diluted to 10 percent concentration. Regardless of concentration, all preparations are applied to the areas of hyperpigmentation two or three times daily until the desired degree of depigmentation is obtained. In general, the lower the concentration of monobenzone, the longer will be the period of time required to achieve this result. All therapy should be discontinued if no results are apparent after 4 months. After successful depigmentation, the application of the drug twice weekly may be sufficient for maintenance therapy.

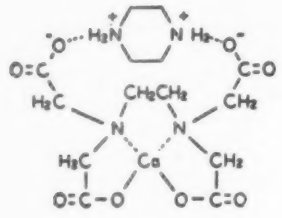
Applicable commercial name: Benoquin.
Paul B. Elder Company cooperated by furnishing scientific data to aid in the evaluation of monobenzone.
J. Am. Med. Assoc. 162:974 (Nov. 3) 1956.

Preparations

Ointment Monobenzone (Benoquin) 20 percent; 1¼ ounce tubes and 1 pound jars.

Piperazine Calcium Edathamil — Perin®

PIPERAZINE CALCIUM EDATHAMIL is a chelated compound produced by reacting edathamil with calcium carbonate and piperazine.—The structural formula of piperazine calcium edathamil may be represented as follows:



Actions and Uses

Piperazine calcium edathamil is proposed for the treatment of pinworms (Enterobius vermicularis) and roundworms (Ascaris lumbricoides) on the basis of its piperazine content. Large amounts of the chelated compound are relatively nontoxic to laboratory animals. Likewise, there have been no reports of toxic reactions to date after administration of therapeutic doses to man. On the basis of limited clinical experience, it would appear that the chelated form is of the same order of effectiveness as the citrate and tartrate salts of piperazine. (See the monograph on piperazine citrate.)

Dosage

Piperazine calcium edathamil is administered orally. Dosage is expressed in terms of the hydrous base, piperazine hexahydrate. The proposed dosage for pinworms in children or adults is 75 mg. per kilogram of body weight per day, administered at one time or in two divided doses for a period of 15 days. Dosage for smaller children and infants is reduced according to weight. For roundworms, a one-day course of treatment consisting of 100 mg. per kilogram of body weight is proposed. Further clinical evidence is necessary to establish the lowest optimum dosage of piperazine calcium edathamil.

Preparations for use as stated for the foregoing drug are marketed under the following name: Perin.
Endo Laboratories, Inc., cooperated by furnishing scientific data to aid in the evaluation of piperazine calcium edathamil.
J. Am. Med. Assoc. 162:658 (Oct. 13) 1956.

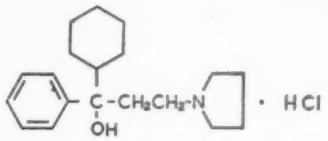
Preparations

Syrup Piperazine Calcium Edathamil (Perin) 500 mg. per 5 ml.

Procyclidine Hydrochloride

Kemadrin® Hydrochloride

PROCYCLIDINE HYDROCHLORIDE is 1-cyclohexyl-1-phenyl-3-pyrrolidino-1-propanol hydrochloride.—The structural formula of procyclidine hydrochloride may be represented as follows:



Actions and Uses

Procyclidine hydrochloride, a synthetic aminopropanol, is related in chemical structure and pharmacological action to cycrimine hydrochloride and trihexyphenidyl hydrochloride. Thus, the drug exerts predominantly atropine-like actions on parasympathetic-innervated peripheral structures and a pronounced antispasmodic effect on smooth muscle. It also relieves spasticity in voluntary muscle groups, the latter action forming the basis of its clinical use.

Procyclidine hydrochloride is employed for the symptomatic treatment of paralysis agitans (Parkinson's disease). It is as effective for this purpose as the hydrochloride salts of cycrimine and trihexyphenidyl. Thus, the drug is more useful for reducing muscle rigidity in postencephalitic Parkinsonism than in the arteriosclerotic or idiopathic types of the disease. Effect on tremor is variable; in general, tremor is reduced, although in some severely spastic cases this symptom can become exaggerated as rigidity is relieved. For patients with severe tremor and advanced rigidity, the combination of procyclidine with other antispastic drugs may be advisable.

On the basis of laboratory studies and clinical experience thus far, it would appear that the toxicity of procyclidine hydrochloride is not significant. Side-effects are typical of those produced by parasympatholytic drugs and include dryness of the mouth, mydriasis, lightheadedness, and disorientation. Gastric upsets are also produced occasionally. The frequency, duration, and intensity of these side-effects are chiefly a function of dosage and at clinical levels consist usually only of dryness of the mouth. The drug should be administered cautiously to all patients with glaucoma, tachycardia, and urinary retention.

Dosage

Procyclidine hydrochloride is administered orally. Dosage is variable depending on the age of the patient

New **Potentiated Pain Relief**

A.P.C. WITH Demerol®

Tablets

Each tablet contains

Aspirin	200 mg. (3 grains)
Phenacetin	150 mg. (2½ grains)
Caffeine	30 mg. (½ grain)
Demerol® hydrochloride	30 mg. (½ grain)

Average Adult Dose... 1 or 2 tablets repeated in three or four hours as needed.

- ***marked potentiation of analgesia***

plus

- *mild sedation*
- *antispasmodic action*
- *antipyretic action*
- *no constipation*
- *no interference with micturition*

"Such a combination has proved clinically to be far more effective and no more toxic than equivalent doses of any of these used singly."

Bonica, J.J.; and Backup, P.H. (Tacoma General Hospital, Washington): *Northwest Med.*, 54:22, Jan., 1955.

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and the cause of the disease. In general, younger patients and those who have had encephalitis require and tolerate a higher dosage than do older patients and those with arteriosclerotic or idiopathic Parkinsonism. The usual initial dose is 7.5 mg. per day administered in three divided doses after meals. This may then be gradually increased to 15 to 30 mg. per day. Doses as high as 45 to 60 mg. daily have been employed, usually without undue side-effects.

Applicable commercial name: Kemadrin.

Burroughs Wellcome & Company, Inc., cooperated by furnishing scientific data to aid in the evaluation of procyclidine hydrochloride.

J. Am. Med. Assoc. 162:1057 (Nov. 10) 1956.

Preparations

Tablets Procyclidine (Kemadrin) Hydrochloride 5 mg.

Report to the Council

The Council has authorized publication of the following report from the Committee on Toxicology.

H. D. KAUTZ, M.D., *Secretary.*

The following report is a summary of the 1956 annual meeting of the Committee on Toxicology. These proceedings have been digested in order to bring to the medical profession timely reports on subjects that might not otherwise come to the readers' attention. Certain of the more important topics considered and actions taken thereon by the Committee are set forth.

BERNARD E. CONLEY, *Secretary*
Committee on Toxicology.

Committee On Toxicology

Annual Meeting

The Committee on Toxicology held its annual meeting on March 29, 1956, at the headquarters of the American Medical Association, Dr. Torald Sollmann, Chairman, presiding. In addition to the Chairman and Secretary, the following members were present: Drs. J. M. Arena, H. B. Haag, A. J. Lehman, E. Press, and Mr. J. C. Ward. In addition to headquarter's representatives, Drs. E. W. Constable, State Chemist, North Carolina; K. P. DuBois, Toxicity Laboratory, University of Chicago; and W. J. Hays and S. W. Simmons, United States Public Health Service, attended as guests of the Committee.

Abstracted reports of some of the more important discussions and actions follow:

Kerosene Poisoning.—A subcommittee on poisoning by kerosene was appointed to study measures for improved safety in the use of petroleum distillates. Progress was reported on current projects to develop a monograph on kerosene poisoning and to promote precautionary labeling. Proposals for the clinical evaluation of various methods of treatment and laboratory investigation of methods for determining amounts of absorbed kerosene were discussed. The Committee agreed to join the American Academy of Pediatrics and the American Public Health Association in a joint clinical study of the treatment of poisoning by kerosene and petroleum distillate.

Exploitation of Nonprescription Drugs.—During the past year, several instances potentially harmful to the public health, especially that of children, have occurred. Representative situations include promotion of a clown-shaped medicine bottle designed to attract children to the container, promotion of vitamin pills on a children's program in a manner appealing to the toddler's tastes for sweets, and distribution of aspirin by vending machines. Since drugs cause 20% of the accidental deaths (33% in children under 5 years) and 22% of the suicides from nongaseous poisons, the Committee feels compelled to comment on these developments.

Devices intended to tempt children to accept drugs as something other than medication can have only unfortunate consequences. Medicine containers designed as toys tempt the very young to take freely of their contents. Vending machines for the automatic dispensing of aspirin, vitamins, and other nonprescription drugs are subject to the same censure. Such machines operate unattended, and children cannot be expected to discriminate between those that dispense gum and candy and those that dispense drugs. Accordingly, the Committee moved that it be placed on record as against the use of vending machines for drugs in public places accessible to children and others lacking in mature judgment.

Poison: Definition and List.—The Committee has been repeatedly asked to define and enumerate substances that it considers poisonous. To this end, definitions of poison presented in 11 current textbooks on pharmacology and medical jurisprudence submitted by 25 leading pharmacologists and representative legal definitions of 16 national and local government agencies in this country and abroad were collected and examined.

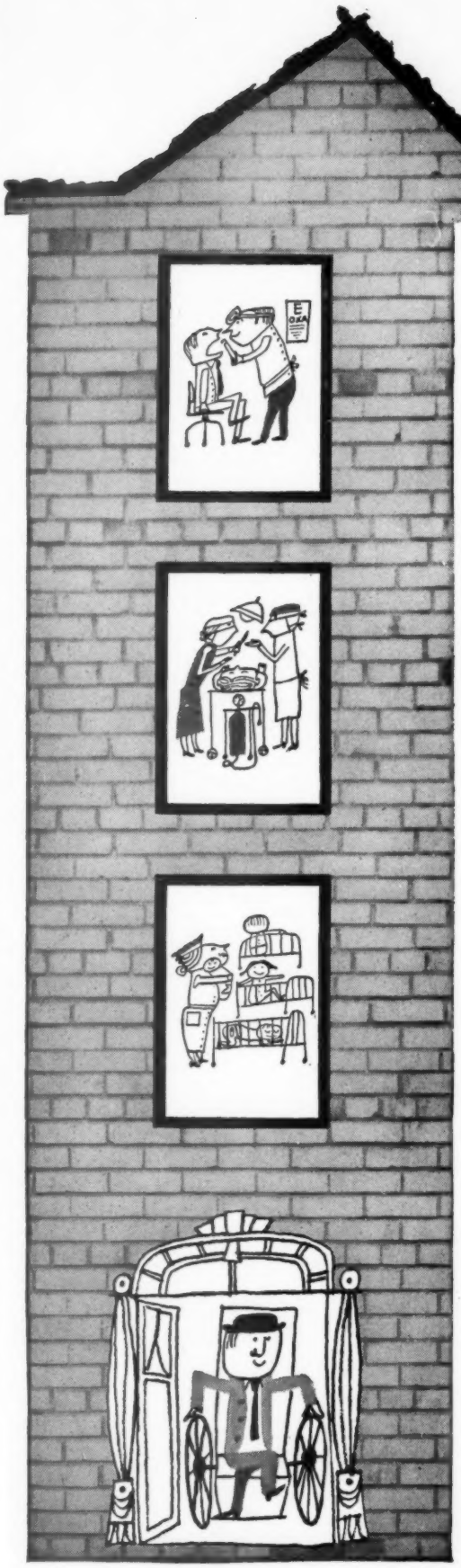
There is no uniformity of legal or scientific opinion as to what constitutes a poison. Various laws, both state and national, vary widely in their definitions. Statutes that employ dosage values vary in their specifications from 5 grains to 5 gm. as the "destructive," "deadly," or "fatal" quantity for "(adult) human life." Those state laws not utilizing a quantitative definition employ vague, indefinite, and generally unsatisfactory terms such as "noxious," "deleterious," or "virulent poisons" to specific chemicals classed as poisons.

Since a precise definition that would fit all circumstances is not possible, the Committee felt that any substance that, when improperly used, may produce harm by chemical action should be provided with an appropriate precautionary label statement. Such precautionary statements should provide warnings for different categories of hazards.

A list of several hundred poisonous substances compiled from legal and trade sources in this country and abroad is also under consideration for adoption.

Public Education About Poisons.—A report of a conference between a Committee representative and school health workers in Richmond, Va., was given regarding means for education of the public about poisons. The school health workers felt that a variety of approaches should be used, such as poster contests on chemical safety and distribution of pamphlets similar to those given away during Fire Prevention Week. They felt that the 30 million school children could be made watchdogs for chemical safety.

The value of radio and television programs presented in such form as to be appealing to both children and parents was stressed. Local chapters of the American Red Cross and the Parent-Teacher Association were mentioned as organizations through which instruction in the home hazards of chemicals could be emphasized. The use of the Committee's exhibit at health fairs and the broadcast of its radio transcription on accidental poisoning over local radio stations were mentioned. A permanent subcommittee was appointed



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to continue this study of means for improving education of the public in chemical safety.

Poison-Control Centers.—A status report on the activities of 13 of 17 operating centers was made to the Committee. Several thousand cases of poisoning have been compiled by the various centers, only one of which had been in operation more than one year. Although most of the centers are experiencing problems peculiar to activities that depend on voluntary and part-time help, there is hope that centralizing some of the duties associated with compiling information and keeping records might ease their growing pains. The feasibility of establishing a central agency to provide information to centers and to tabulate their poisoning cases is presently being investigated.

J. Am. Med. Assoc. **162**:973 (Nov. 3) 1956.

Report to the Council

The Council has authorized publication of the following report.

H. D. KAUTZ, M.D., *Secretary*

It is generally recognized that the final evaluation of the toxicity of a chemical encountered by humans should be in terms of its effect on man. The following report concerns the first experimental study of the storage, excretion, and possible clinical effects in man of chlorophenothane (DDT) given in many small daily doses. By relating excretion to dosage, the study makes practical the quantitative estimation of the dosage for persons with extensive occupational exposure to DDT, and thus eventually makes possible evaluation of the effect of DDT on man after years of exposure. This is important, for DDT continues as the predominant residual insecticide for agricultural and public health use. Any effects of repeated exposure would appear on the average most promptly, most frequently, most diversely, and most severely among persons whose exposure has been long and intensive.

BERNARD E. CONLEY, *Secretary*
Committee on Pesticides.

Chlorophenothane (DDT)

The Effect Of Known Repeated Oral Doses Of In Man

WAYLAND J. HAYES Jr. M.D.
WILLIAM F. DURHAM, Ph.D.
and
CIPRIANO CUETO Jr., B.S., Savannah, Ga.

Much knowledge is available regarding the effect of repeated doses of chlorophenothane (DDT) on a variety of animals. Significant interspecies variation has been found in its toxicity when given orally, the storage of DDT in fat, and the conversion of DDT to 1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethylene (DDE). Some other aspects of the pharmacology of DDT have not been investigated sufficiently to determine whether interspecies differences are present. A final evaluation of the effect of DDT on man must be made with human subjects. The practical importance of the problem is evident from the fact that a greater tonnage of DDT than of any other insecticide is used in agriculture, that DDT occurs regularly in prepared means,[1] and that it is stored in the fat of most persons in the general population.[2]

From the Communicable Disease Center, Public Health Service, U. S. Department of Health, Education, and Welfare.

Read before the American Association for the Advancement of Science, Panel Discussion on Hazardous Household Chemicals and Agricultural Poisons, sponsored by the Committee on Toxicology and the Committee on Pesticides, American Medical Association, Atlanta, Ga., Dec. 29, 1955.

An investigation was designed with the following objectives: 1. Study of possible clinical effects of different dosage levels. Only those dosage rates were chosen that were estimated to be harmless for it was not the purpose of the study to cause illness. The highest dosage rate chosen (0.5 mg. per kilogram of body weight per day) is about 200 times greater than the dosage to which the general population is exposed (0.0026 mg. per kilogram per day) but 5 times less than the smallest dosage that is estimated to cause transient, mild sickness (2.5 mg. per kilogram per day). This latter estimate was made on the basis of animal experiments and on the basis of the smallest single dose of DDT known to produce mild illness in man.[3] This estimate should not be confused with the dosage of 2.5 mg. per day (about 0.035 mg. per kilogram per day), which Fitzhugh estimated could be ingested for long periods without injury.[4] 2. Determination of the relationship between oral dosage of DDT and the storage of DDT-related compounds in adipose tissue at equilibrium. Improvement made in chemical methods during the study permitted a third objective to be added: 3. Determination of the relationship between oral dosage of DDT and the urinary excretion of bis(*p*-chlorophenyl) acetic acid (DDA).

Permission was obtained from the Bureau of Prisons, U. S. Department of Justice, to carry out the experiment using volunteers in a federal correctional institution. The study was explained to almost the whole population of the institution. Detailed explanations were made to those who were interested in participating. The men who tentatively volunteered were examined and were accepted if they proved to be qualified physically and in other ways. The fact that participation was at all times strictly voluntary must be emphasized; each man was free to leave the study at any time.

METHODS

The selected volunteers were divided into six groups, three entering the study in February, 1954, and three in May, 1954. As shown in table 1, groups 1 to 3 received dosages of 0, 3.5, and 35 mg. of DDT per man per day, respectively, for periods ranging up to 18 months. Each dose was carried in a capsule of oil containing the appropriate concentration of recrystallized *p,p'*-isomer of DDT.

Although groups 4, 5, and 6 received the same dosages as groups 1, 2, and 3, respectively, two major changes were made: technical DDT was used, and it was administered as an emulsion in milk rather than in capsules. The capsules were originally chosen for groups 1 to 3 because of their convenience. They were abandoned for groups 4 to 6 in favor of a formulation more nearly like a "natural" residue and also for administrative reasons. The emulsion concentrates were prepared by homogenizing 5 gm. of gum arabic, 90 cc. of water, 10 cc. of 95% ethyl alcohol, and 15 cc. of peanut oil. For groups 5 and 6, the peanut oil moiety of the formulation contained 0.538 and 5.38% of technical DDT respectively. These concentrations were chosen in order that 5 cc. of the two emulsion concentrates would contain 3.5 and 35 mg. of DDT respectively. Before being offered to the men, 5 cc. of the appropriate emulsion concentrate was diluted with milk to a total volume of about 2 oz. Chemical analyses of capsules and emulsions gave values for the concentration of DDT that were in excellent agreement

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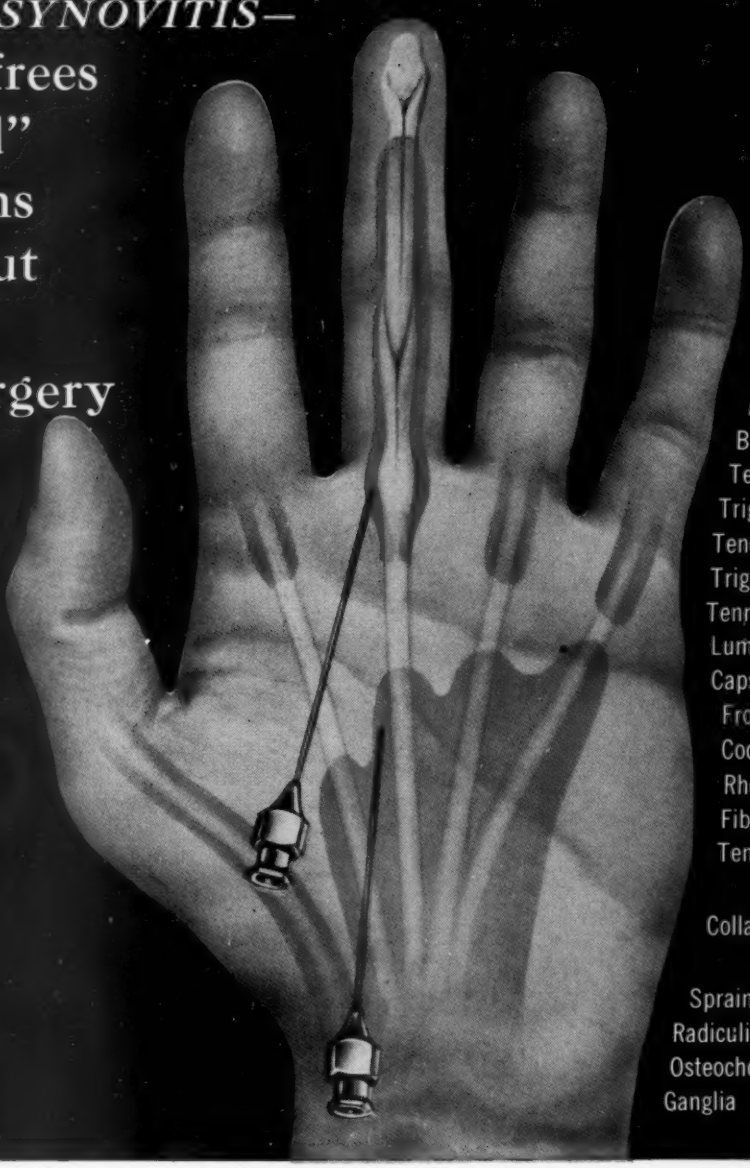

Osteoarthritis
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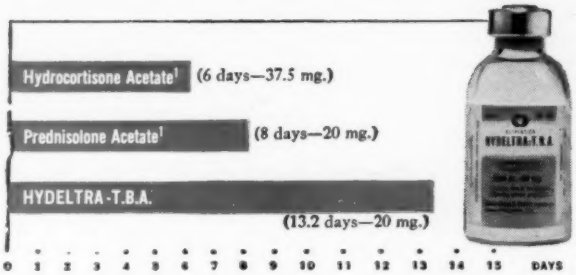
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Prednisolone Acetate[1] (8 days—20 mg.)
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1. Hollander, J. L., *Paper read at conference in New York City, May 31 and June 1, 1955*

with intended values. Analyses indicated that the emulsions were stable in DDT content for at least two months, a longer period than that required for the experiment, because new supplies of emulsion were prepared at monthly intervals.

Proper dosage for the different groups of men was assured by packaging each capsule and marking each bottle of emulsion for individual volunteers. The capsules, regardless of their DDT content, were identical in appearance. The same was true of the emulsions.

TABLE 1.—*Outline of Experiment*

Type of DDT	Group No.	Dosage: Added, Mg./Man/Day	Dosage: Total (Range),* Mg./Kg./Day	Case No.	No. of Men: Entering Experiment	Completing 17 Predosage Days	Completing 1 Mo. of Dosage	Completing 12 Mo. of Dosage	Completing 18 Mo. of Dosage	Completing Final Examinations
Recrystallised	1	0	0.0021-0.0031	0-8	9	8	7	1	0	5
	2	3.5	0.048-0.059	9-16	8	8	7	1	0	4
	3	35	0.41-0.61	17-25	9	9	8	1	1	7
Technical	4	0	0.0023-0.0034	26-33	8	8	6	3	1	4
	5	3.5	0.038-0.063	34-41	8	8	8	2	0	8
	6	35	0.36-0.57	42-50	9	8	8	6	3	7
Total					51	47	44	14	5	35

* The total dosage included dietary DDT as well as the administered dose. Dietary DDT, resulting from agricultural residues, was estimated at 0.184 mg./man/day on the basis of the analyses of whole meals. The total dosage varied somewhat according to the weight of the men.

The men were told the dosage rates and the design of the experiment before they volunteered, but no volunteer was told his individual dosage. Furthermore, this detail was not revealed to the medical officer stationed at the institution nor to the medical technical assistants. All of the volunteers, irrespective of group, were given capsules (or emulsion) containing no DDT for 17 days at the beginning of the study; the regular doses were begun without notice.

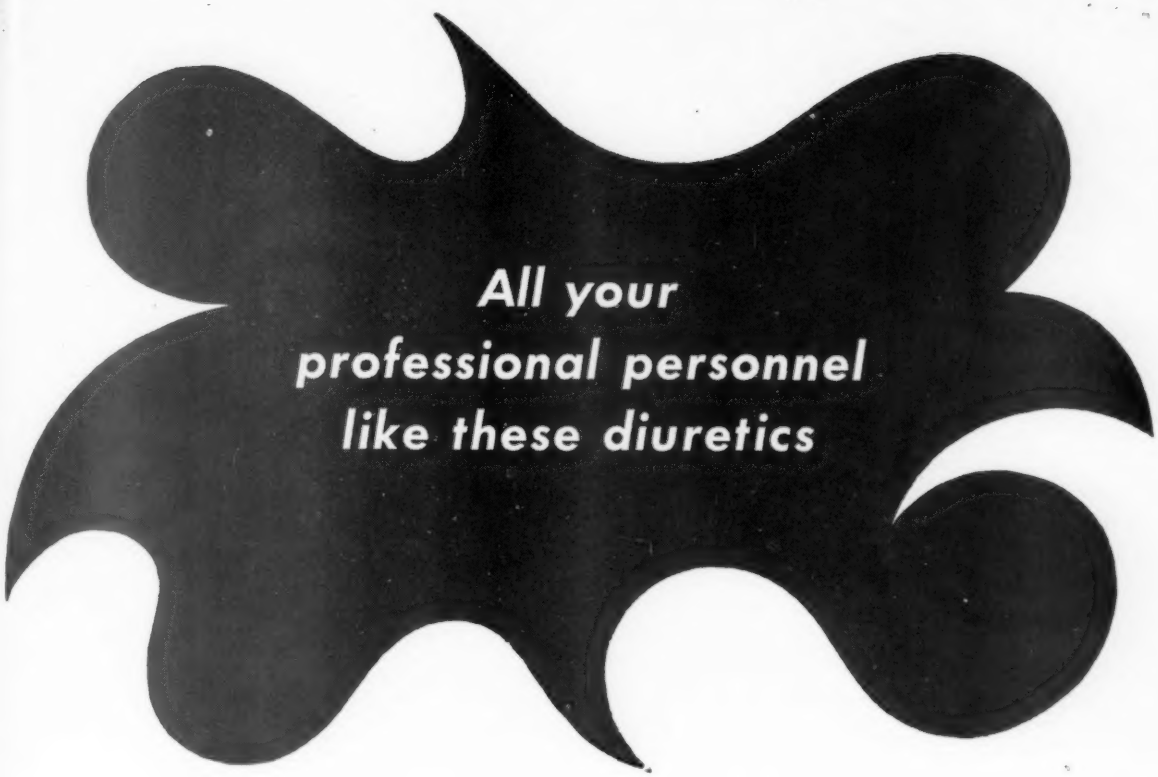
TABLE 2.—*DDT and DDE Found in Typical Meals Served to Volunteers*

Meal	Date, 1954	Total Found, Mcg.: DDT	DDE
Morning			
1	Aug. 25	115.6	16.9
2	Oct. 4	45.1	18.9
3	Nov. 9	54.9	6.8
4	Dec. 9	79.0	33.9
Mean		73.7	19.1
Noon			
1	Aug. 25	204.0	24.8
2	Oct. 4	44.6	23.0
3	Nov. 9	21.6	6.0
4	Dec. 9	26.5	4.1
Mean		74.2	14.5
Evening			
1	Aug. 25	72.5	22.0
2	Oct. 4	51.3	17.2
3	Nov. 9	22.7	16.3
4	Dec. 9	69.1	11.8
Mean		54.2	16.8
Daily Mean		202.1	50.4

Samples of the meals served the men in the dining hall were analyzed for DDT content to determine the exposure that might be expected from this source. Complete meals for a total of four days were analyzed. The results are shown in table 2. Considerable variation was found among foods and even among whole meals with respect to DDT content; however, the mean daily DDT intake of 0.202 mg. was in reasonable agreement with the value of 0.184 mg. reported by Walker and co-workers[1] for a larger series of sample meals. The value of 0.184 mg. per man per day was used in computing the total daily DDT dosage for each man shown in table 1, because this value is based on a large number of samples and is the best estimate of the true average now available. This is especially true because the figures in table 2 would agree better with those given by Walker and his colleagues if it were not for the values obtained for breakfast and especially lunch on Aug. 25. The value for the breakfast was associated with the finding of 69.6 ppm of DDT in stewed dried fruit. Except for bread, which showed a concentration of 100.9 ppm of DDT, the DDT content of the lunch was not unusual. There was no record of the kind of shortening used in this bread; however, it was later learned that bread, all of which was baked at the institution, was occasionally made with lard (which contained, on analysis, a relatively high concentration of DDT) rather than with vegetable shortening (which proved to be of low DDT content). In both the fruit and the bread the DDE concentration was relatively low.

Volunteers were checked for previous exposure to insecticides (which in all instances was negligible) and were given a careful symptoms review, a general physical examination, and a variety of laboratory tests prior to their entrance into the project and at six-months intervals thereafter. Particular emphasis was given to the neurological examination and liver function tests, since in experimental animals the major effects of DDT are on the nervous system and the liver. The liver function tests carried out were sulfobromophthalein retention and plasma cholinesterase level. The electrometric method of Michel[5] was used for the cholinesterase determination. Vorhaus and co-workers[6] have shown that plasma cholinesterase level is a significant index of hepatic function. Preliminary studies with monkeys have indicated that some decrease in plasma cholinesterase level might be associated with high DDT dosage levels.

In all instances, fat samples for the determination of DDT-derived compounds were obtained by biopsy, using local procaine anesthesia. Blocking was done around the operative site, and it was generally possible to avoid infiltration of the tissue that was later excised. The biopsy specimen was usually taken through a 1.5-in. incision from the subcutaneous adipose tissue of the abdomen. Body fat content was calculated from specific gravity, which was determined by weighing the individual under water.[7] Analyses for DDT, DDE, and DDA were made by the Schechter-Haller method. The procedure used for adipose tissue has been described by Mattson,[2] and the procedure used for urine has been described by one of us (C.C.).[8]



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During the study some of the men left the institution by transfer or parole or on other authority. Whenever sufficient notice was given, the men were completely reexamined shortly before their participation in the project ended. During the course of the study, 126 complete sets of examinations were carried out on the 51 volunteers. Table 1 indicates the number of men in each group who participated for specific periods. Of the 47 men who remained in the study longer than 17 days, biopsy specimens from 35 were taken, and they were completely reexamined after their last dose of DDT. Two men refused the final biopsy but underwent the other tests. Four others were released on such short notice that no final examination was possible, but a biopsy was performed by a private physician after their release. Thus, of the 47 volunteers, only 6 were discharged in such a way that they received no final biopsy or examination.

TABLE 3.—*Condition of Volunteers at Beginning of Experiment*

	Groups Given Recrystallized p,p'DDT					
Group No.	1		2		3	
No. of Men	8		8		9	
	Range	Mean, S. E.	Range	Mean, S. E.	Range	Mean, S. E.
Age, yr.	22.5-50.1	30.9±3.4	22.4-48.7	29.5±3.1	20.9-45.8	27.8±2.6
Weight, kg.	60-87.7	73.6±3	62.7-77.2	68.6±2	57.7-86.3	74.5±3
Red blood cell count, millions/cu. mm.	4.1-5.5	4.8±0.03	3.9-5.6	4.8±0.05	3.0-6.9	4.9±0.04
Hemoglobin level, gm./100 cc.	12.0-14.0	13.3±0.7	13.5-14.5	14.0±0.7	12.0-15.0	13.8±10
White blood cell count, thousands/cu. mm.	5.4-15.0	9.0±1.0	6.9-9.9	8.6±0.4	5.9-13.8	9.2±1.0
Polymorphonuclear neutrophil leukocytes, %	37-71	55±5	40-71	58±4	42-66	57±2
Heart rate, rest, strokes/min.	60-88	72±3	64-100	78±5	64-96	88±3
Heart rate, exercise, strokes/min.	80-120	99±5	80-136	104±6	92-120	105±4
Heart rate, exercise and rest, strokes/min.*	−12 to+8	−3.2	−12 to+16	−2.3	−16 to+4	−5.4
Systolic blood pressure, rest, mm. Hg	105-152	120±5	100-134	115±4	100-140	121±4
Pulse pressure, rest, mm. Hg	28-55	39±4	35-70	47±2	30-65	46±4
Systolic blood pressure, exercise, mm. Hg	105-150	121±5	98-130	117±4	105-160	127±7
Pulse pressure, exercise, mm. Hg	25-55	41±4	28-65	47±5	35-85	58±6
Plasma cholinesterase, ΔpH/hr.	0.54-1.07	0.84±0.08	0.53-1.10	0.86±0.07	0.60-0.96	0.69±0.04
DDT in fat, ppm.	3-9	6.9±0.8	4-11	6.1±0.8	4-9	6.6±0.7
DDE in fat, ppm.	7-26	14.9±2.8	7-16	10.8±1.3	8-19	12.2±1.3

	Groups Receiving Technical DDT					
Group No.	4		5		6	
No. of Men	8		8		9	
	Range	Mean, S. E.	Range	Mean, S. E.	Range	Mean, S. E.
Age, yr.	22.9-40.4	28.9±2.0	21.7-33.6	27.5±1.4	22.7-34.8	27.9±1.3
Weight, kg.	58.6-81.3	70.4±3	58.1-97.2	74.5±5	62.2-97.7	75±2
Red blood cell count, millions/cu. mm.	4.5-7.2	5.3±0.05	4.4-6.3	5.1±0.07	4.8-5.6	5.2±0.06
Hemoglobin level, gm./100 cc.	13.0-14.5	13.7±0.6	13.0-15.0	13.4±0.8	13.0-15.5	14.1±0.9
White blood cell count, thousands/cu. mm.	5.9-10.7	8.2±0.8	5.6-9.9	7.9±0.8	4.4-11.1	8.3±0.8
Polymorphonuclear neutrophil leukocytes, %	35-68	52±3	38-63	50±3	46-75	59±3
Heart rate, rest, strokes/min.	56-76	65±3	60-80	72±2	64-88	76±3
Heart rate, exercise, strokes/min.	80-136	98±7	80-116	98±4	104-136	116±4
Heart rate, exercise and rest, strokes/min.*	−8 to+20	−1.0	−20 to+8	−1.0	−4 to+24	+4.8
Systolic blood pressure, rest, mm. Hg	98-140	118±5	112-135	122±3	115-130	122±2
Pulse pressure, rest, mm. Hg	24-50	38±4	35-65	49±3	31-53	46±2
Systolic blood pressure, exercise, mm. Hg	102-140	118±5	118-135	120±2	112-135	123±3
Pulse pressure, exercise, mm. Hg	30-52	41±3	35-65	49±3	36-65	48±3
Plasma cholinesterase, ΔpH/hr.	0.72-1.37	0.91±0.09	0.56-1.35	0.88±0.09	0.70-1.04	0.86±0.03
DDT in fat, ppm.	4-13	9.5±1.0	7-11	8.5±0.6	4-12	7.2±1.0
DDE in fat, ppm.	5-15	10.2±1.2	7-13	10.4±0.8	2-22	8.6±2.0

*Recorded as increase or decrease of strokes per minute compared to the rate for the same person just before exercise followed by 2 min. of rest.

RESULTS

Condition of Volunteers at Start of Experiment.—The condition of the volunteers on entering the experiment is shown in part in table 3. The men who entered in February varied in age from just under 21 to just over 50 years; those who entered in May varied from just over 21 to a little over 40. All the men except three were essentially normal, not only regarding values shown in table 3 but in other respects as well. Two of the abnormal men (cases 7 and 29) were in control groups and, therefore, not subject to any influence of DDT. They were asymptomatic and afebrile throughout. The patient in case 7 had a white blood cell count that varied from 13,400 to 20,200 per cubic millimeter over a period of several months. He showed as high as 12% of eosinophils, but the differential count was otherwise normal. There was moderate lymphadenopathy. Despite a thorough examination, the underlying cause of the difficulty was not determined. It was established that leukemia was not present. The patient in case 29 had albuminuria and microscopic and other findings consistent with a diagnosis of latent chronic nephritis. Illness did not progress in either subject during the study; in fact, the condition of the patient in case 7 returned toward normal.

The third subject (case 9) had abnormally high sulfobromophthalein retention on initial examination; his plasma cholinesterase value was within normal limits. He received 3.5 mg. of DDT per day and was asymptomatic during the 89 days he remained in the experiment. Because of inadequate notice of his departure from the institution, no final studies were done on this man.

Two volunteers who gave a history consistent with infectious hepatitis were taken into the experiment despite the effect of very large doses of DDT on the liver of experimental animals and, according to one author,[9] of man. One man (case 5), a control patient, received no DDT; the other (case 20) received 35 mg. of DDT per day. Jaundice did not recur in these men, and they showed no abnormality in liver function tests during the experiment.

Effect on Health.—Four men quit the experiment of their own accord. One subject (case 0) quit one day after the first biopsy; thus, except for the biopsy, he was not part of the experiment. A second man (case 8) from the same control group considered that his health had been injured after a total of 182 days in the study (no DDT given). He refused a final biopsy. Physical and laboratory examination disclosed no abnormality except a dermatitis of the right leg, which he attributed to his participation. A volunteer (case 16) who received 3.5 mg. of DDT per day also refused a final biopsy and quit just before he was transferred from the institution. He had participated for 155 days and had received 138 doses of DDT. He had several complaints, including pain every day in every bone, occasional headache, and tearing of the right eye. He submitted to complete physical and

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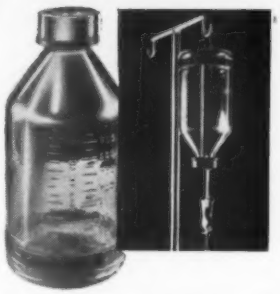

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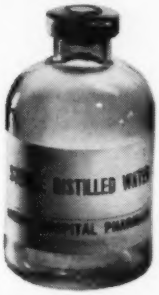

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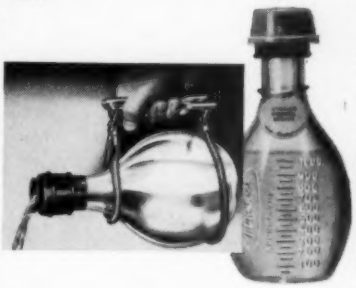

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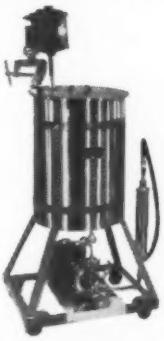

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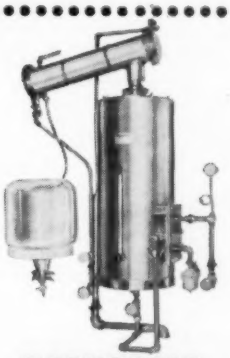

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laboratory examination, and all findings were normal. His complaints obviously were of psychoneurotic origin, and even the man himself did not seem to take them seriously. One volunteer (case 19) receiving 35 mg. of DDT per day quit after 21 days (DDT given last 4 days). He had no specific complaints but was unwilling to continue.

Of the total of 37 volunteers who were questioned specifically on the matter just after completion of their participation in the study, only the two mentioned considered that their health had been adversely affected. In one instance of weight loss, the possibility of injury caused by DDT exposure was considered. The subject (case 11) had a history of a 7 kg. (15 lb.) fluctuation of weight before entering the experiment. His weight loss of 6 kg. (13 lb.) during the study was associated directly with hard physical work in a hot environment. He accepted this explanation and, with the onset of cool weather, regained his weight while continuing to take DDT.

Changes in certain important items that can be measured were tabulated and compared for the six groups for the periods 5 to 6, 7 to 8, 9 to 10, 11 to 12, and 12 or more months of dosage respectively. It was necessary to tabulate changes rather than observed values because, as some men completed their participation, the composition of the sample shifted. For example, the average weight of men in group 1 was less after five or six months than at the beginning of the experiment because a heavy man had dropped out; most of the men who remained had gained weight, and the average change of weight was a slight gain. The items examined in this way were weight,

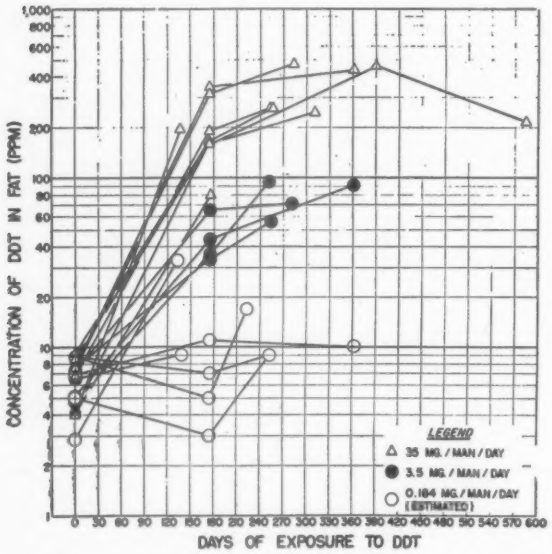

Fig. 1.—Storage of DDT in the subcutaneous fat of volunteers given indicated doses of recrystallized *p,p'*-isomer of DDT.

hemoglobin level, red blood cell count, white blood cell count, percentage of polymorphonuclear leukocytes, heart rate (at rest, just after exercise, and after two minutes of rest), systolic blood pressure and pulse pressure (at rest and after exercise followed by two minutes of rest), and plasma cholinesterase level. Although changes were observed in all of these values, none were correlated consistently with increased dosage of DDT or with increased duration of exposure. Since the changes were random in distribution and not unusual in degree, they must be attributed to normal variation. No significant change in sulfobromophthalein retention was noted. This item was not tabulated because the retention values for most of the men were zero before and after exposure to DDT. In a similar way, chest x-ray findings were not tabulated, for they all were essentially normal.

The initial review of symptoms revealed a great variety of minor complaints. These complaints were not unusual, and the men undoubtedly were predisposed to some of them by their confinement. A small number of minor physical defects was revealed by examination.

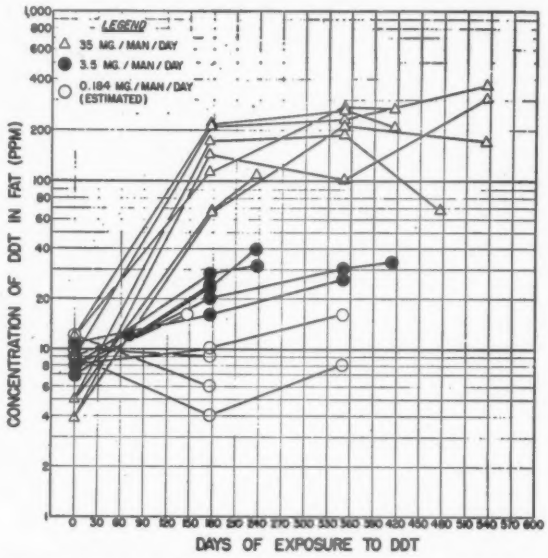

Fig. 2.—Storage of DDT in the subcutaneous fat of volunteers given indicated doses of technical DDT.

In subsequent examinations no increase or significant change in abnormal physical findings was discovered. There was some tendency for the volunteers to give fewer complaints at subsequent interviews.

Results of following tests were taken into consideration in the neurological examination: gait, including ability to walk on toes and heels; coordination including Romberg, finger to nose, heel to shin, adiadochokinesia, rebound, past-pointing, tremor, handwriting, and "tongue twisters"; deep reflexes, superficial reflexes, and clonus; muscle strength, including all major movements of the neck, shoulder, elbow, wrist, fingers, hip, knee, and ankle; sensation, including light touch, pinprick, two-point discrimination, position sense, vibration sense, stereognosis, and differentiation of heat and cold; and function of the cranial nerves, including identification of an odor, visual fields, reactivity of pupils, extraocular movements, strength of bite, sensation of the face, coordination and strength of facial muscles, hearing, pharyngeal reflex and voice, and protrusion of the tongue. All of the participants remained normal in regard to these neurological tests; of particular interest, they showed no loss of coordination and no indication of tremor.

In contrast to the random and normal variation encountered in other tests, the values for the storage and excretion of DDT-derived materials showed a strong correlation with dosage and with duration of exposure. In conclusion, during the entire study, no volunteer

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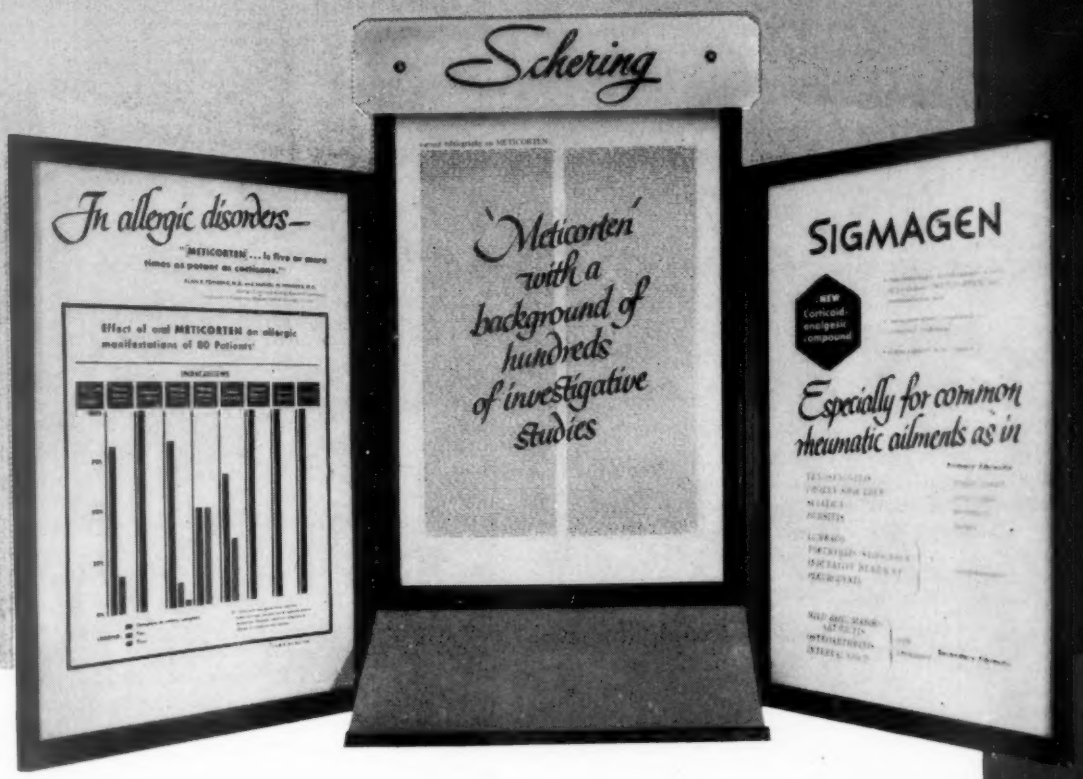
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complained of any symptom or showed any sign of illness that did not have an easily recognized cause clearly unrelated to exposure to DDT.

Storage of DDT-Derived Materials.—The storage of DDT in subcutaneous fat by groups 1, 2, and 3 is shown in figure 1 and that by groups 4, 5, and 6 in figure 2. It is clear that storage was directly proportional to dosage. The graphs suggest that, at the dosages used, human males achieve storage equilibrium necessary to establish this conclusion firmly. The absolute variation was greater among the higher storage for DDT in about a year, but further observation is level values, but, as shown by a comparison of the

TABLE 4.—*Variability of Storage of DDT at Different Storage Levels*

		Duration of Exposure, Mo.					
		0		6		12	
Group*	No. of Men	Mean Storage, Ppm	$V_{\bar{x}}$,† %	Mean Storage, Ppm	$V_{\bar{x}}$,† %	Mean Storage, Ppm	$V_{\bar{x}}$,† %
3	8	6.5	10.0	202	15.3	...	...
6	6	7.7	20.2	155	15.6	210	12.0

* For each group, the same persons were considered in each calculation.
† Coefficient of variation of the standard error of the mean.

coefficients of variation in table 4, the relative variation remained about the same.

An unexpected finding was the difference in the amount of storage at the same dosage in connection with recrystallized DDT and technical DDT respectively. Rats show a difference in this regard, but it is

TABLE 5.—*Statistical Significance of Differences in DDT Storage in Human Fat Associated with Dosage, Duration of Exposure, and Type of DDT*

Condition	Comparison	Statistical Level of Difference, %	
		Duration of Exposure, Mo.	
Type of DDT	Dosage, Mg./Man/Day	3-6	7-18
Technical	0 vs. 3.5	<95	>99
	3.5 vs. 35	>99	>99
Recrystallized	0 vs. 3.5	>99	>99
	3.5 vs. 35	>99	>99
		Dosage, Mg./Man/Day	
Type of DDT	Duration of Exposure, Mo	3.5	35
Technical	0 vs. 3-6	99	>99
	3-6 vs. 7-18	>99	>95
Recrystallized	0 vs. 3-6	>99	99
	3-6 vs. 7-18	>99	>95
		Dosage, Mg./Man/Day	
Duration of Exposure, Mo.	Type of DDT	3.5	35
3-6	Tech. vs. Recryst.	>99	<90
7-18	Tech. vs. Recryst.	>99	>95

smaller in degree and opposite in direction; that is, under conditions of equal exposure, rats store more technical DDT than recrystallized DDT. At a dosage of about 0.5 mg. per kilogram of body weight per day for 10 months or more, the volunteers stored recrystallized DDT in their fat at a concentration of 216 to 466 ppm (mean, 340 ppm). At the same dosage for the same period, other volunteers stored technical DDT at a concentration of 101 to 367 ppm (mean, 234 ppm). Unfortunately, it is impossible to determine whether the difference was associated with the character of the DDT samples or with the formulations in which they were administered. As shown in table 5, however, the level of statistical significance for the difference between the storage of recrystallized and of technical DDT is very nearly as great as the significance of differences based on dosage and on duration of exposure calculated in the same way. These latter differences, of course, have a simple, biological explanation. The statistical analysis indicates that the difference between the storage of recrystallized and of technical DDT cannot be ignored but should be the subject of further studies in the hope that a reasonable biological and/or chemical explanation may be found.

Storage of DDE in subcutaneous fat is shown in table 3 and figure 3. In the presence of ordinary dietary exposure to DDT, the storage of DDE showed about

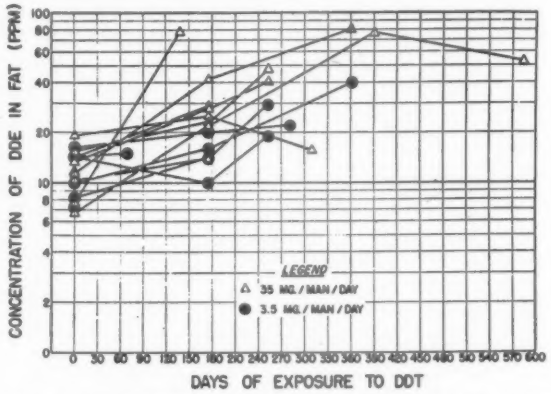

Fig. 3.—Storage of DDE in the subcutaneous fat of volunteers given indicated doses of recrystallized *p,p'*-isomer of DDT. For graphic clarity, values for the control group have not been plotted.

the same variability as the storage of DDT. For the men entering the experiment the average storage of DDE was 11.2 ±0.74 ppm, giving a coefficient of variation for the standard error of 6.0%; the average storage of DDT was 7.4 ±0.37, giving a coefficient of variation of 5.0%. Men who ate recrystallized DDT showed a definite increase in the absolute amount of DDE stored. After six months at a dosage of 35 mg. per man per day, eight men showed an average DDE storage of 32.6 ±7.0 ppm as compared to 12.3 ±1.5 ppm for the same individuals upon entering the experiment. There was a further increase of DDE storage during additional months of exposure; however, DDT was stored in so much greater concentrations that the relative storage of DDE decreased sharply. Thus, after six months at a dosage of 35 mg. per man per day, eight men stored only 14% of their total DDT-derived material in the form of DDE, as compared to 65% for the same persons at the beginning of the experiment.

TABLE 6.—*Variability in Fat Storage of DDT Expressed on the Basis of Concentration and Total Amount Stored*

			DDT Storage in Fat			
			Concentration		Total Amount	
Duration of Exposure, Mo.	Daily DDT Dosage, Mg.	No. of Men	Mean, Ppm	$V_{\bar{x}}$,* %	Mean, Gm.	$V_{\bar{x}}$,* %
	0	4	8.5	18.0	0.109	14.0
5.9	3.5	5	25.2	15.9	0.354	11.8
	35	9	167.0	17.9	2.245	15.5
	0	3	11.6	24.1	0.152	26.9
11.5-12.9	3.5	4	44.0	34.1	0.613	23.2
	35	8	270.0	15.9	3.280	15.2

* Coefficient of variation of the standard error of the mean.

The storage of DDE by men who ate technical DDT presented a different picture. Until 18 months of exposure, there was no clear evidence that those men stored any more DDE after exposure than they did

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before; however, at 18 months, the only three samples available showed DDE concentrations of 85, 42, and 28 ppm. Although these values constituted only 16% of the total storage of DDT-derived material, they are all well above average for general population figures and thus indicate the conversion of technical DDT to DDE in the volunteers. The question is complicated by the fact that the chemical method does not permit measurement of DDE when it constitutes less than 10% of the total DDT-derived material in the eluate from the chromatographic column. It is possible that a limitation of the chemical methodology may account for the apparent difference in the way in which human beings handle recrystallized DDT and technical DDT.

No conclusion can be reached regarding the time at which equilibrium is reached in the storage of DDE. Figure 3 might be thought to suggest the establishment of equilibrium at about a year, but the number of values available for comparison is very small. In animals, it generally requires longer to establish storage equilibrium for DDE than for DDT.

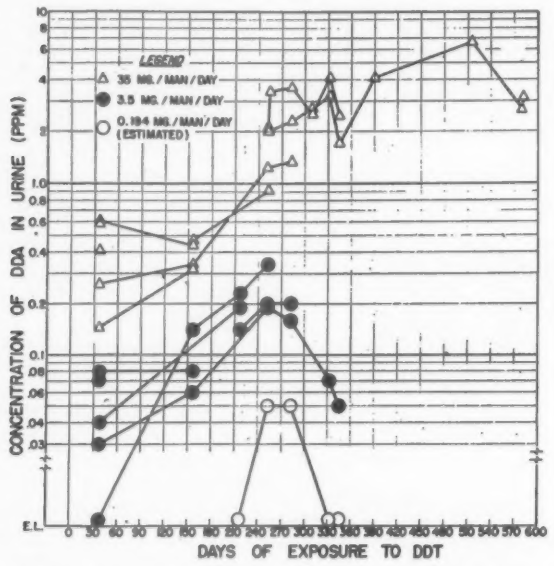

Fig. 4.—Urinary excretion of DDA by men given indicated dosage of recrystallized p,p'-isomer of DDT. E. L. = experimental limit, a concentration too small to be detected by the available chemical method.

As an alternative to the use of concentration as a measure of DDT storage, the total amount of DDT stored per man was considered. This value was determined by multiplying the weight of the subject's body fat by the concentration of DDT in his fat. In table 6, the results of this study are shown. It is apparent from inspection of the coefficients of variation that the intergroup differences were about the same, using either DDT concentration in fat or total DDT content as a measure of the magnitude of DDT storage. The average total DDT storage for the highest dosage group after 12 months of exposure was 3.28 gm., based on measured concentration of DDT in fat and estimated total body fat. This average total storage would represent a potential DDT dosage to the average man (70 kg.) of 47 mg. per kilogram. It is unrealistic to suppose that fat would ever be metabolized rapidly enough to cause acute clinical DDT poisoning when the total available dosage is 50 mg. per kilogram or less.

In single specimens of blood taken from 4 men who had received 599 or more doses at the highest rate, DDT was found at a concentration of 1.6 to 4.2 ppm or an average of 2.8 ppm. DDE was found in these specimens at concentrations of 1.3 to 3.1 ppm or an average of 1.9 ppm. In the individual samples, DDE constituted 34 to 45% of the total DDT-derived material. Specimens of saliva collected the same day from the same 4 men contained no detectable DDT-derived material. Results were also negative for a single specimen of bile diluted with intestinal juice.

Excretion of DDT-Derived Materials.—Urinary excretion of DDA is shown in figures 4 and 5. The study of urinary excretion was exploratory at first. The method for isolating DDA from urine was perfected during the course of the experiment.[8] For this reason, the early values are considered less accurate than the later ones; even so, certain conclusions are justified. The daily ingestion of 3.5 mg. or more of DDT led to the excretion of substantial amounts of DDA in about 30 days. There were no values to indicate how early excretion might be detected regularly; however, even subjects with only dietary exposure to DDT occasionally excreted DDA at concentrations that approached 0.2 ppm, indicating a distinct relation between DDT dosage and the amount of DDA excretion. The excretion of DDA also increased with the duration of DDT exposure. The highest concentration of DDA observed in a single sample was 9.6 ppm. Of particular interest was the study of 24-hour urine samples recorded in table 7. These samples show the marked variation of

TABLE 7.—*Recovery of DDA from Twenty-Four-Hour Urine Specimens from Volunteers Who Had Received DDT at the Rate of Thirty-Five Milligrams per Man per Day for Sixteen or More Months*

Group no.		3	6	6	6	6
Case no.		25	44	46	47	49
Concentration of DDA ppm	Oct. 3	2.70	7.04	1.66	2.55	3.08
	Oct. 4	3.12	2.04	0.45	0.77	2.08
	Nov. 29	...	...	...	1.06	5.90
	Nov. 30	...	...	...	2.80	5.60
	Mean	2.91	4.54	4.06	1.79	4.16
	S.E.	0.21	2.50	2.38	0.51	0.94
Concentration of DDA, V$\bar{x}$,* %		7	55	59	29	23
Amount of DDT-equivalent,† mg./24 hr.	Oct. 3	7.35	7.23	8.80	6.30	6.40
	Oct. 4	6.47	6.34	9.61	4.76	5.56
	Nov. 29	...	...	...	5.39	5.65
	Nov. 30	...	...	...	7.48	5.86
	Mean	6.91	6.78	9.20	5.98	5.87
	S.E.	0.47	0.48	0.41	0.63	0.19
Amount of DDT, V$\bar{x}$,* %		7	7	4	11	3

* Coefficient of variation of the standard error of the mean.
† (Mg./kg. of DDA) × (kg. of urine) × 1.26. This latter factor (the dividend obtained by dividing the molecular weight of DDT by the molecular weight of DDA) serves to convert DDA values to DDT equivalent values.

DDA concentration characteristic of samples collected at a single voiding. When the concentration was multiplied by volume to give total DDA content in milligrams, the variation was reduced. Thus, considering all observed values, the coefficient of variation for DDA concentration was 16.3%, whereas that for total DDA content of the same samples was only 5.4%. The variation between samples of urine from a given man taken on different days tended to be about the same as the variation between samples from different men taken on the same day. The specific gravity of urine samples tends to be inversely proportional to the volume; however, the variation in DDA concentration values for urine samples collected at a single voiding could not be decreased significantly by adjusting the values in accordance with the specific gravity of the various samples. In view of the results with 24-hour

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Ref.: Deeb, E. N. & Vitagliano, G.R.: A. Rev. Tuber. & Pul. Dis.: 72,543-7 (Oct. '55)

samples, this may indicate that the excretion of DDA does not parallel that of sodium chloride and other solids, which play a major role in the determination of specific gravity.

Expressed as DDT, the DDA found in the 24-hour urine samples varied from 4.8 to 9.6 mg, and averaged 6.7 mg. per sample. Thus, after storage equilibrium had been achieved, it was possible, through urinary excretion, to account for 13.6 to 27.4% or an average of 19.0% of the entire ingested dose. Figures 4 and especially 5 suggest that equilibrium of DDA excretion is reached in about a year. A specimen of feces from a man at the highest dosage level contained DDT (2.6 ppm) and DDE (2.7 ppm). Difficulty with isolating DDT-derived material from human feces is great, especially with the acid fraction (DDA and related materials). DDA was not demonstrated, but its presence, or the presence of related material, is not excluded.

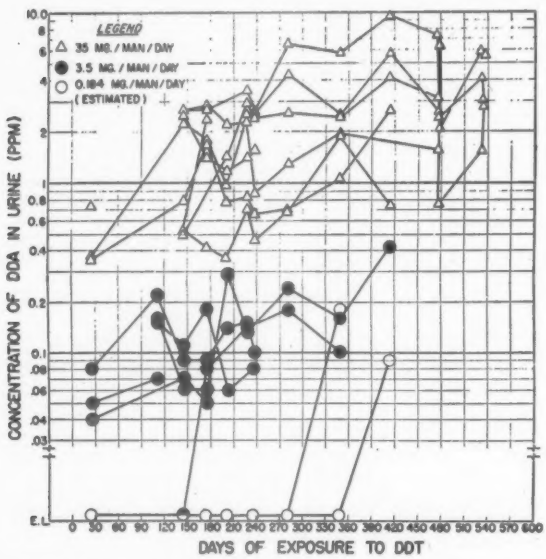

Fig. 5.—Urinary excretion of DDA by men given indicated dosage of technical DDT. E. L. = experimental limit, a concentration too small to be detected by the available chemical method.

Comment

As shown in table 8, the median storage of DDT found in the volunteers before they entered the experiment corresponded well with that reported by Laug and co-workers[10] for a series of samples collected from the general population sometime before 1951. Laug and his colleagues did not distinguish DDE. The estimation of DDT reported in that paper is more comparable with the estimation of DDT in the present paper than with the estimation of DDT plus DDE. The distribution of the present values for DDT storage differs from the distribution reported by Laug in that the more recent work shows a concentration of figures near the mean and no values at all corresponding to Laug's high and low ranges. This difference in distribution may be explained by a more constant and more controlled use of DDT in agriculture at the present time. Earlier use of the pesticide was more sporadic and may have been less well regulated. The difference in distribution may also be related to differences in chemical method. Early unpublished studies carried

TABLE 8.—*Range of Concentration of DDT Found in Human Fat*

Range, Ppm DDT	Cases, %	
	Laug Report	This Study
0.0	20	0
0.1-1.0	9	0
1.1-5.0	28	25
5.1-10.0	28	61
10.1-20.0	12	14
Over 20.0	3	0

out in this laboratory at about the same time as those of Laug show the same distribution and general magnitude of values as those reported by Laug. These early studies involved sufficient differences in chemical method from those now used that it is difficult to evaluate the results. Interpretation of early zero values appears especially difficult.

The concentration of DDT stored in the fat of the volunteers at apparent equilibrium after the highest dosage was almost as high as that for one man with extensive occupational exposure who showed 648 ppm of DDT and 434 ppm of DDE. The DDE stored by the volunteers constituted only an average of 16% or less of their total DDT-derived material, whereas the corresponding value for the man with occupational exposure was 40%. The difference was probably related to the duration of high exposure—18 months or less for the group and five years for the worker.

Summary and Conclusions

With full knowledge of the plan of the study and with complete freedom to withdraw at any time, 51 men volunteered to take daily, oral doses of DDT for different intervals. One-third of the men received no DDT except that in the ordinary diet; one-third received 3.5 mg. per man per day; and one-third received 35 mg. per man per day, which is about 200 times the daily rate at which an average man receives DDT from his diet. During the entire study, no volunteer complained of any symptom or showed, by the tests used, any sign of illness that did not have an easily recognized cause clearly unrelated to exposure to DDT.

The storage of DDT in man is proportional to dosage. There was an unexplained difference in the storage of recrystallized and of technical DDT. The pure material was stored in fat at an average concentration of 340 ppm and the technical material at an average concentration of 234 ppm after an identical dosage of 35 mg. per man per day. It appears that, at the dosages used, human males achieve maximum storage of DDT in about a year and thereafter store no more of the material despite continued intake. Men who ate DDT showed an absolute increase in the storage of DDE. No conclusion could be reached regarding the time at which equilibrium is reached in the storage of DDE. The storage of DDT and the storage of DDE show about the same relative variation (co-efficient of variation) at different dosage levels but the absolute variation is, of course, greater at higher dosages.

A method for determining the concentration of DDA in urine was perfected during the course of the study. The excretion of DDA is proportional to the dosage of DDT. This makes possible an objective measurement of DDT absorption by the determination of DDA in urine and greatly expands the possibility of practical study of formulators and others who

SF CAPSULES: 250 mg. plus vitamins.

SF ORAL SUSPENSION: 125 mg. per 5 cc. plus vitamins.

SURGICAL POWDER: 200 mg. per Gm., 5 Gm. vial.

CAPSULES: 50, 100, and 250 mg.

TABLETS: 50, 100, and 250 mg.

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EAR SOLUTION (0.5%): 10 cc. dropper bottle.

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25

have occupational exposure to DDT. It was possible to account for about 20% of the DDT administered, in terms of DDA excreted in the urine. The results indicated that a large safety factor is associated with DDT as it now occurs in the general diet.

The chlorophenothane (DDT) capsules were supplied by R. P. Scherer Corporation, Detroit.

J. Am. Med. Assoc. 162:890 (Oct. 27) 1956.

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calendar of meetings 1957

NEW ENGLAND HOSPITAL COUNCIL (including New England Council of Hospital Pharmacists)—March 25-27, Boston, Massachusetts. (Statler Hotel)

MIDWEST HOSPITAL ASSOCIATION (includes Hospital Pharmacy Section)—April 24-26, Kansas City, Missouri. (Municipal Auditorium)

SOUTHEASTERN HOSPITAL CONFERENCE (includes Southeastern Society of Hospital Pharmacists)—April 24-26, Atlanta, Georgia. (Atlanta-Biltmore Hotel)

PRE-CONVENTION CONFERENCE ON PARENTERAL PRODUCTS (conducted by the Philadelphia Hospital Pharmacists' Association)—April 27, New York City. (Hotel Statler)

AMERICAN PHARMACEUTICAL ASSOCIATION—April 28-May 3, New York City. (Hotel Statler)

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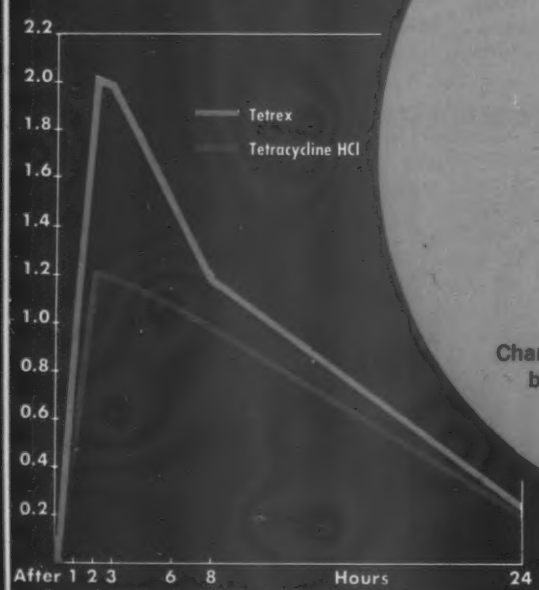

OOD LEVELS AFTER SINGLE DOSE

Tet

TETRACYCLIN PHO

Chart (left) shows blood levels practically double with Tetrex

— from 3 independent studies by P. A. Bunn, M.D., Sol Katz, M.D., and G. A. Cronk, M.D., on 188 patients

AMERICAN SOCIETY OF HOSPITAL PHARMACISTS—April 28-30, New York City. (Hotel Statler)

TRI-STATE HOSPITAL ASSOCIATION—April 29-May 2, Chicago, Illinois. (Palmer House)

ASSOCIATION OF WESTERN HOSPITALS—May 6-9, Los Angeles, California. (Statler Hotel)

CATHOLIC HOSPITAL ASSOCIATION—May 27-30, Cleveland, Ohio. (Statler Hotel)

INSTITUTE FOR HOSPITAL PHARMACISTS, CATHOLIC HOSPITAL ASSOCIATION—May 25-28, Cleveland, Ohio. (Municipal Auditorium)

AMERICAN MEDICAL ASSOCIATION—June 3-7, New York City.

INSTITUTE ON HOSPITAL PHARMACY (American Hospital Association)—June 24-28, Seattle, Washington.

RADIOISOTOPE TECHNIQUES COURSE, Co-sponsored by the Philadelphia College of Pharmacy and Science and the Philadelphia Hospital Pharmacists' Association—June 28, Philadelphia, Pennsylvania.

PREPARATION OF PARENTERAL PRODUCTS COURSE, Co-sponsored by Philadelphia College of Pharmacy and Science and the Philadelphia Hospital Pharmacists' Association—June 17-28 and July 8-19, Philadelphia, Pennsylvania.

INSTITUTE ON HOSPITAL PHARMACY (American Hospital Association)—August 18-23, Chicago, Illinois

AMERICAN HOSPITAL ASSOCIATION—September 30-October 3, Atlantic City, New Jersey. (Convention Hall)

ASSOCIATION OF MILITARY SURGEONS. October 28-30, Washington, D. C. (Hotel Statler)

FOURTH PAN AMERICAN CONGRESS OF PHARMACY AND BIOCHEMISTRY—November 3-8, Washington, D.C.

MARYLAND-DISTRICT OF COLUMBIA-DELAWARE HOSPITAL ASSOCIATION (includes Hospital Pharmacy Section)—November 18-20, Washington, D. C. (Shoreham Hotel)

AMERICAN MEDICAL ASSOCIATION (Clinical Meeting)—December 3-6, Philadelphia, Pennsylvania.

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE (includes Pharmacy Section)—December, Indianapolis, Indiana.

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LETTERS

The Hospital Formulary System

DEAR SIRS: The "Hospital Formulary" is curcently a controversial subject. At our hospital we definitely feel that the formulary is not to our advantage. I have written the following as an argument for those who are opposed to it. Would you consider it for your publication?

There are many types of hospitals—mental, general, surgical, obstetrical, etc., some private and some tax supported. Therefore, for accreditation purposes, will the compulsory formulary system be forced upon all of us, or will we, as individual institutions, be allowed to accept or reject this formulary system?

Today's literature leads the reader to believe that his institution *must* use a formulary system to receive accreditation. For those who sincerely believe that the formulary would *not* fit into their pharmaceutical service, this is a concerning problem.

I am a pharmacist who is the Secretary of the Pharmacy and Therapeutics Committee in our hospital. I sincerely believe that the Pharmacy and Therapeutics Committee is a worthwhile endeavor and support it fully.

For those who have not had the opportunity of reading the recommended procedures that this committee must follow, may I say that of ten suggestions only one concerns a formulary.

For the record, let us say that our Pharmacy and Therapeutics Committee is concerning itself with the problems of investigational drugs, drugs stocked on the floors, diagnostic procedures, (literature) available to the nursing stations, and civil defense procedures.

You can see we have purposely withheld work on a formulary. I say, "purposely," subjectively, because of unanimous agreement.

Our hospital is presently training 14 medical interns and 8 residents. Our staff is fully cooperative with the pharmacy and our visiting staff (which I believe is the largest in the city) is also cooperative. We unanimously agreed that at this time a formulary at our hospital would breed discontent and tend to "wreck" the excellent spirit of our staff.

Let's get down to the bottom of this matter as concerns the everyday function of the pharmacy. If we run a "clean house"—by this I mean sensible buying, an efficient dispensing system, and sufficient product information available to all concerned—what is the big question all about? In other words, if everyone is happy, why must we upset the applecart?

Must we, who are operating with no objections at all, force a formulary on our staff simply for the concern of accreditation?

JOHN W. MURPHY, *Hospital Pharmacist*
St. Louis, Missouri

Appreciates Bulletin

DEAR SIRS: Many thanks for your courtesy and helpfulness in sending us a copy of the September-October (1955) issue of THE BULLETIN of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS. The article of particular interest was Gladhart, Wood and Purdum on "Bacteriostatic Agents."

Again, many thanks for your courtesies.

HARRY O. BURKS

Bilhuber-Knoll Corp.
Orange, New Jersey

From Italy

DEAR SIRS: I have been following the articles and notes appearing in the very fine BULLETIN OF THE AMERICAN SOCIETY OF HOSPITAL PHARMACISTS with the highest interest and would most willingly have them diffused and made known to our Italian colleagues.

Therefore, may I ask you to send your authorization so that I can have them either partly or wholly republished in our company's Bulletin, while of course referring to the source and author.

On the other hand, I should be glad for you to use the information and articles contained in our Bulletin in your SOCIETY's publication.

I look forward to hearing from you and thank you in advance.

GIUSEPPE MARTINI, *Vice-Director*
Bollettino Della, Societa
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EDITORIAL

Substitution and the Formulary System

by Don E. Francke

The National Pharmaceutical Council is said to be planning to devote its major efforts this year to combatting methods used by hospitals to solve the product duplication problem. These methods, the National Pharmaceutical Council implies, involve substitution. In view of this, hospital pharmacists, administrators, physicians, and members of the Pharmacy and Therapeutics Committees will be interested in the following editorial which is reprinted from The Bulletin of the American Society of Hospital Pharmacists 13:23 (Jan.-Feb.) 1956.

Hospital pharmacists in institutions which operate under the formulary system are sometimes accused of substitution. In these instances, use of the term substitution is limited to the dispensing of a different brand than is called for on the prescription, rather than to the broader meaning of the term which involves the dispensing of a drug which is a different chemical entity than that prescribed.

Hospital pharmacists do dispense brands other than those called for on the prescription. So do retail pharmacists under certain circumstances. Is this, then, not substitution, pure and simple? The answer is no. Any pharmacist, whether in retail or hospital practice, may at any time dispense a different brand of a drug with the knowledge and permission of the physician. This is one of the basic professional prerogatives of all pharmacists.

Hospital pharmacists do not dispense a different brand of a drug unless they are specifically authorized to do so. In hospitals operating under the formulary system, this authorization is obtained in writing from the medical staff. Drugs are accepted by their generic names and the pharmacist is authorized to dispense any one of a number of selected and approved brands of a given drug. In no case is there any intent or effort to deceive the physician. In fact, authority for the adoption of the formulary system arises from the medical staff; it is not a unilateral policy adopted and implemented by the pharmacy department.

The formulary system is not substitution for the same reason that product duplication is not product imitation. The element of deception is not involved in either the formulary system or in product duplication. In contrast, intent to deceive is paramount in both substitution and product imitation. The substitutor gives a product other than the one prescribed, without the knowledge or consent of the physician. The product imitator manufactures a preparation which resembles in size, color, shape, and/or taste the product of another manufacturer. The product imitation is produced with the specific intent to deceive, to be used without the knowledge of the physician in place of the product it seeks to imitate.

On the other hand, the formulary system involves no intent or desire to deceive. It is a system promulgated and agreed upon by members of the medical staff, a system implemented with their consent and operated with their knowledge. Deception is in no way involved.

Neither is deception involved with product duplication. Here a manufacturer produces a drug to capture a portion of the market, to engage in open competition with other manufacturers. Product duplication is often unwise, often works to the detriment of manufacturers who have done the basic work on a drug, often handicaps those pharmacists who of necessity must stock numerous brands of a drug, often tends to weaken or to destroy the very concept of brand names which manufacturers seek to promote — but it is never deceitful.

It is true that there is a relationship between the formulary system and product duplication. In fact, the formulary system is at present the only rational and effective answer to this problem and one which works well in hospitals. It is doubtful that it would be desirable or practical in retail practice. It is suitable to hospital practice for several reasons: 1. Physicians can decide whether or not the system is adopted; 2. If dissatisfied, they can change the policy to full recognition of individual brand names; 3. The pharmacist and medical staff have a close working relationship with well established lines of organization and communication which insures understanding cooperation; and 4. The formulary system is but part of a total plan designed to promote rational therapy in hospitals.

However, there is no relationship between the formulary system and product imitation. Hospital pharmacists have no desire to further the cause of those who manufacture imitation products.

The formulary system does not involve substitution. It, like product duplication, does not involve deception: It is a policy originated by and operated with the written approval of the medical staff.

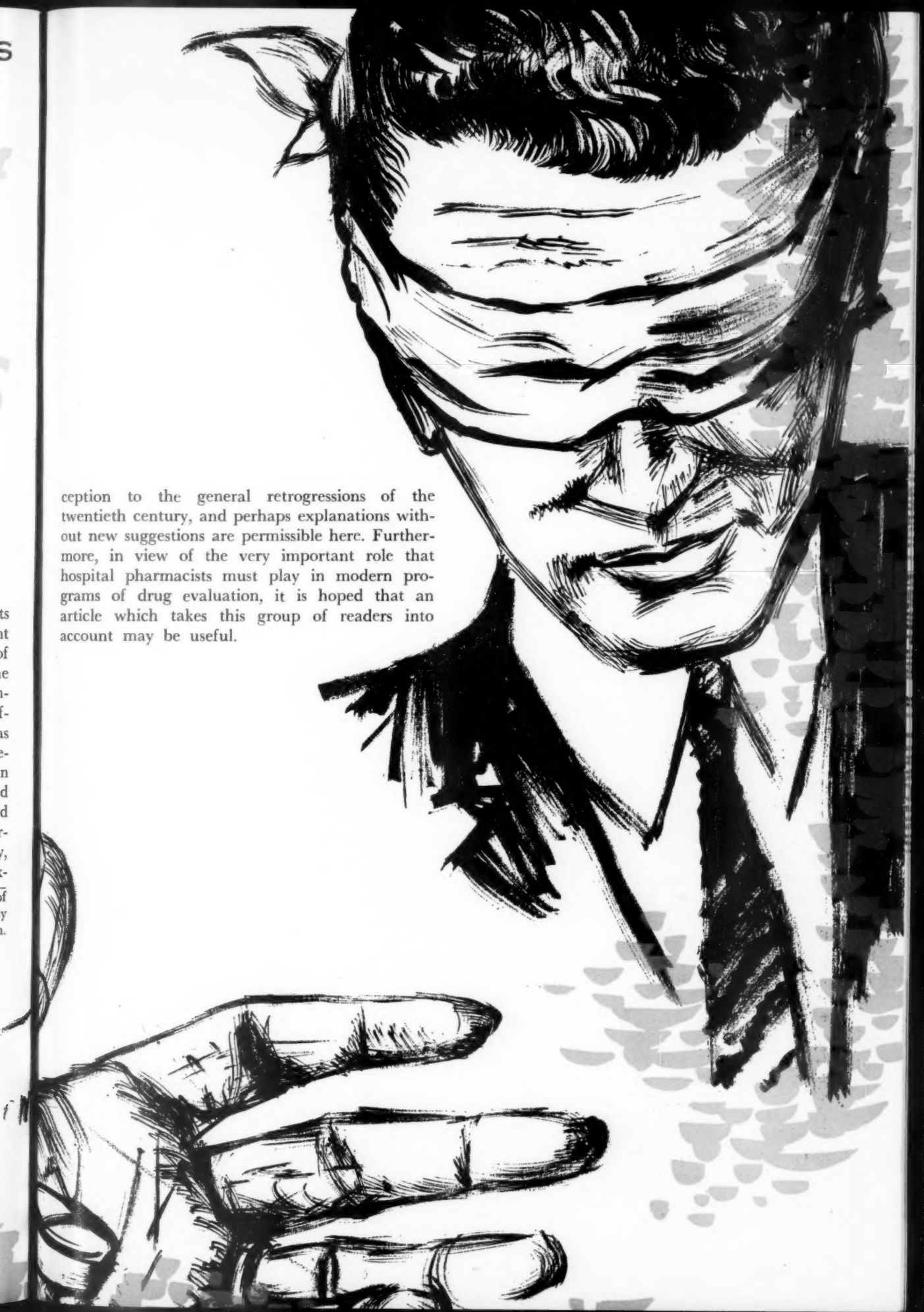
IMPORTANT CONSIDERATIONS IN THE evaluation of NEW DRUGS

by EDWARD A. CARR, JR.

THE FOLLOWING DISCUSSION of certain aspects of the evaluation of new drugs, in the present state of our knowledge, is more of a review of the past and present than a suggestion for the future. It must therefore be presented with considerable humility. In politics, international affairs, etc., certain writers, greatly venerated as pundits, are making their living by writing detailed analyses, pointing out that the world is in a very bad state—a not particularly profound observation. These long discussions, which end up with no suggestions of any use, are not particularly rewarding to the reader. Fortunately, medical advances represent an encouraging ex-

EDWARD A. CARR, JR., M.D. is Assistant Professor of Pharmacology and Internal Medicine at the University Hospital, University of Michigan, Ann Arbor, Michigan.

ception to the general retrogressions of the twentieth century, and perhaps explanations without new suggestions are permissible here. Furthermore, in view of the very important role that hospital pharmacists must play in modern programs of drug evaluation, it is hoped that an article which takes this group of readers into account may be useful.



Role of Clinical Impression

Long before "scientific" evaluators began to study the problem, practitioners of medicine obtained a surprisingly accurate idea of the value or lack of value of various remedies. The virtues of substances derived from the opium poppy in the relief of pain, the value of quinine, etc., were recognized by those who cared for sick persons, and a tremendous number of worthless remedies have after a period of time been discarded. The success of "clinical impression" should not surprise us, for the principle of "clinical impression" is exactly the same as the principle of the type of drug evaluation which we now think of as "scientific." In other words, the value of a new drug, or indeed of any type of treatment, is judged by comparing the results obtained among patients receiving the new treatment with the results to be expected if they had not received such treatment. The expected results are, of course, based on experience obtained, either at the same time or in the past, with another group of patients who are, ideally, similar to the treated group in every respect except that they did not receive the new treatment. In practice it is, of course, impossible to achieve this ideal, *i.e.* the two groups are never completely similar in all respects except the treatment in question, but the more closely this ideal is approached, the more valid the results of the comparison will be. Serious deviations from this principle are a particularly common source of error in "clinical impressions." Although the clinician often cannot remember all the details of the various patients whom he has treated with other methods before using the one in question, his impression that these people did better or worse than those now receiving the new treatment may turn out to be a correct one. This rough and ready clinical method is sometimes much more feasible than stricter methods of evaluation and is free of the ethical problems which always confront one when he is deliberately planning an experiment involving human beings. On the other hand, the stricter methods of drug evaluation, which we shall discuss in the rest of this article, though more difficult and troublesome to set up, often give a speedier, safer, more accurate and more precise answer than the "clinical impression." However, it should be repeated that the method of "clinical impression," though often inaccurate and less efficient than the methods discussed below, can over a period of time lead to entirely valid results, as it is based upon the same principle as the stricter methods discussed below. There is no justification for an attitude of snobbishness toward the "clinical impression." On the other hand, it is equally true that there is no justification for the assumption that the method of "clinical impression" is completely adequate for our needs. It is sometimes stated that a very large difference between the incidence of success in a new treatment and the incidence of success in an old treatment will immediately become apparent to any experienced clinician. The argument then runs that, inasmuch as startlingly successful new treatment will become immediately accepted and only such new treatments are worth adopting anyway, there is no need for more precise evaluation. The fallacy in this argument lies in the assumption that only tremendous improvements in medical treatment are worth considering. It is obvious that a very small difference in the treatment of an extremely common disease, for example, may result in the saving of thousands of lives over a period of a few years. Such a small difference may require the careful methods of evaluation discussed below for detection.

Reasonable Criteria

Of course, when one is comparing drugs the question of "straining" must be considered carefully. If one "strains", that is, demands too much of a new drug, then he may cause even a useful drug to appear unsatisfactory. On the other hand, if too little is demanded of a drug, it may not have a chance to show its superiority over former methods of treatment. For example, in a study conducted at three American medical schools,[1] trichloroethanol was compared with chloral hydrate as a hypnotic. Using as a criterion the induction of sleep within one hour, two of the groups found no difference between the two drugs. The study at the third medical school did indicate some difference between the drugs. The point here is that if the induction time had been shortened to perhaps 30 or 45 minutes, a difference between these two drugs might have appeared much more definitely. As the test was actually conducted, the drug which was somewhat slower in inducing sleep still had a chance to meet successfully the criterion of induction of sleep within one hour. On the other hand, it is

obvious that if the investigators had demanded that the drugs, when given by mouth, induce sleep within five minutes, they would again have shown no difference between the drugs, as both of them would have failed completely. It should also be noted that the one group in the above study that was able to show a difference in rapidity of induction when trichloroethanol was compared to chloral hydrate, could show this difference only when the medication was not given in capsule form. When the medication was given in capsule form, then none of the medical school groups was able to show any difference between the drugs. This is a good example of the important role of the hospital pharmacist in this type of study. His knowledge of different medication forms and the effects they may have on such matters as rapidity of action of a drug can be very useful to those planning this type of study. Pharmacists are also particularly aware of the importance of dosage in evaluating effects of drugs.

Certain principles of pharmacology have to be taken into account here. If one plots the dose of a drug, usually on a logarithmic scale, against the intensity of response, the resulting dose-response curve is shaped thus: ⟅ . The most accurate determinations can be made in the central, linear portion of the curve where the slope is relatively steep and an error in measuring response will therefore correspond to only a small error in dose. The potency of drugs as measured in animals is therefore commonly expressed as the "effective dose 50 percent," *i.e.* the dose that will cause a response equal to half the maximum possible response achievable by increasing the dose without limit. Drugs can be compared with one another most accurately on the basis of their respective ED_{50}. The difficulty is that often one does not know the ED_{50} in humans. Furthermore, the slope of the aforementioned central part of the dose-response curves of two different drugs may not be parallel and the drugs may therefore be close together in potency in the low dose range and far apart at high doses. Because of the differences in slope of the dose-response curves, it is often advisable to compare the drugs at two different doses. Another useful method is to attempt to estimate the ED_{99}, of one drug, *i.e.* the dose giving 99 percent of the maximum possible therapeutic effect. One then gives this drug at the estimated ED_{99} and determines if the results can be bettered by any tolerated dose of the other drug. It is obvious here that any improvement through the use of the second drug will not be improvement in the number of people affected, as the first drug is already given at the ED_{99}, but in the degree of benefit obtained by those individuals who respond to the drug, or the differences in side effects. In all these considerations, one must be certain that the dose given is well within expected levels of safety.

Importance of Placebos

The pharmacist is in a key position with regard to placebos, *i.e.* "dummy" tablets, solutions, etc, that outwardly appear the same as the drug under test but actually contain only inert material. It is surprising how often the necessity for making the placebo an exact replica of the drug under test is overlooked. Pharmacists are more aware of the importance of vehicles than others tend to be, and such matters as taste, color, etc., are very important in placebos. The necessity for the use of placebos lies in the fact that enthusiasm, on the part of the physician and on the part of the patient, tends to sneak into any trial, even the most carefully conducted. If either the physician or the patient attempts to "lean over backwards" in order to avoid enthusiasm, the study will be biased just as badly in the other direction. It should be noted in passing that, although healthy skepticism is a very desirable trait in anyone conducting clinical evaluations, a healthy skeptic should be skeptical of, among other things, skepticism. Negative enthusiasm is, in some respects, even worse than positive enthusiasm, for it cannot be controlled at all by placebos. In other words, if one is convinced that a certain medication will work, and imparts his enthusiasm to patients, causing them all to feel better, the error will be picked up even when a fundamentally worthless drug is given, as all of the patients receiving only placebos will similarly be improved by the enthusiasm of the physician. One will then have a high success rate for both the placebo and the drug under study, and will know that the study was not valid. On the other hand, if one is convinced in advance that a drug is no good, and the drug is given with such a sour attitude that all of the patients feel worse after they have received it, even though the drug really is effective when given properly, then there will be a poor success rate for both the placebo and the drug. In this instance one will not necessarily know that the study was in error and a fallacious study may

be accepted as perfectly valid, with the unfortunate result that a drug that really was useful is discarded. There is an irrational tendency to feel that a negative result is automatically "more scientific" and therefore more creditable. This is obviously not true. If a present day study gives results in direct contradiction to the apparent experience of previous generations of physicians, it is easily possible that the modern study, by using more refined technics, is indeed correcting a past error. But it is not impossible that in any given case the modern study itself is in error. This consideration unfortunately never dawns on some zealots.

Where objective tests, such as the urinary excretion of some substance produced in the body, can be used the necessity for a placebo is much less. It is undeniable that objective tests have been a tremendous help in the evaluation of drugs and the rapid advances made in certain fields, such as endocrinology and hematology, are probably to a considerable degree associated with the fact that workers in these fields have been able to devise detailed objective tests of function. These tests are by no means to be disparaged. But the necessity for placebos is likely to remain with us for a long time in many fields where objective tests are simply not available. The evaluation of drugs for the relief of pain is a good example. Furthermore, one must be careful when such a test as the urinary excretion of some substance is used as the criterion of improvement; one must be certain that these changes really do correlate with improvement in the clinical state of the patient. After all, the patient himself usually complains of pain, weakness, malaise, etc., and changes in the results of objective tests are important to him only insofar as they imply that the pain, weakness, malaise, etc., will also disappear.

One might think that patients' own reports are too unreliable to be used in studies of this type. In the aforementioned studies on the effect of hypnotics, objective measurements of the induction of sleep, as observed by hospital personnel on the wards, were checked against subjective impressions about the time of induction of sleep, as reported by the patients the next morning. These measurements compared quite well.

There is considerable discussion at the present time concerning the so-called "placebo reactor." A "placebo reactor" is an individual who is particularly affected by suggestion, and therefore is very likely to get a marked effect from a placebo. Certainly in most studies for the evaluation of most new drugs, a considerable proportion of the individuals who receive placebos appears to derive benefits or to suffer side effects from the placebo. It is still not certain that such individuals consistently behave in this way and therefore are entitled to be called "placebo reactors." However, if such individuals do exist, it is important to remember that such an individual is not simply any person who improves without any treatment at all. If the term "placebo reactor" is used, it should be restricted to persons who do not improve in the absence of any medication, but do obtain benefit from placebos. For example, in a study conducted at the Massachusetts General Hospital[2] the effects of pentobarbital, chloral hydrate, and Dormison in inducing sleep were compared. A fourth group of patients received a placebo and a fifth group of patients were controls and received nothing. A certain number of individuals showed effects after the placebo. However, the same proportion of individuals showed effects after receiving no drug at all. It is not correct, therefore, to say that the placebo was effective in inducing sleep. Rather, it is correct, and not in the least surprising, to say that a certain number of people are able to go sleep without any medication.

In considering the question of reaction to placebos, one should also take into account Lasagna's[3] study in which he found that multiple doses of placebo may become decreasingly effective in causing the response he was measuring—relief of pain. In general, the comment most applicable to the placebo is probably that of Abraham Lincoln: "You can fool some of the people all of the time and all of the people some of the time, but you cannot fool all of the people all of the time."

Hospital Pharmacist's Role in Double Blindfold Test

In making up placebos, the pharmacist can also play an important role in arranging that the drugs be given according to some schedule that permits the physician conducting the study to be as ignorant as the patient regarding the exact order in which drugs and placebos are given. This principle of "double blindfold" is of great importance, for it is desirable that the physician be as free from bias as the patient. Of course, physicians should carefully arrange and direct the outline of the study, decide what drugs may be given, decide what type of patient may be used, and in general arrange everything except the final point—the actual order in which drug and placebo are administered. If it would not be safe for a certain patient to receive either the drug or the placebo, such a patient should not be used in the study at all. Once it is assured that any patient in the study can safely be given either drug or placebo, the physician can then delegate to others the arrange-

ment of the actual order in which the drugs are given.

The drugs and placebos must be given in a random manner, not in a haphazard manner. (The distinction between random and haphazard would perhaps require too much space for detailed discussion; as a crude approximation, it might be said that random selection of patients deliberately attempts to insure against bias, whereas haphazard selection simply implies that one does not deliberately insert any bias, and more or less "lets matters take care of themselves," in the hope that the laws of chance will save the study from bias.)

Limitations of Placebos

Digressing for a moment from the matter of drug schedules, it should be noted that besides the matter of safety, simple moral and humanitarian aspects have to be considered very carefully. It is obviously out of the question to withhold effective medication from patients who are suffering agonizing pain. It is similarly out of the question to abandon treatment that is obviously effective in some serious disease and substitute a placebo. Where there exists a serious disease for which reasonably effective treatment is already available, any new treatment that is expected to be an improvement can be compared only with the best effective treatment already known. In serious matters then, a new treatment is compared with the best treatment to date, rather than with placebos. The placebo has its principal usefulness in situations where a considerable number of people are expected to do well without any treatment at all, and a new treatment, in order to be accepted, must show that it can produce considerably better results than those already obtained with no particular therapy at all. On the subject of ethics, however, one point deserves a great deal of stress: When a new therapy becomes available, it is very strongly in the best interest of all patients that the effectiveness or ineffectiveness of this new therapy be established as quickly as possible, be established under the supervision of physicians who are in a position to give close attention to patients receiving such new treatment, and be established under circumstances which permit the toxic effects to be picked up as early as possible. In this way one can quickly discontinue the new therapy, if it begins to have undesirable effects, or can quickly arrange for other patients who are not doing well under usual methods of treatment, to receive the new therapy, if it becomes apparent that the new therapy is going to be of real advantage. This means that such tests should usually be conducted at medical centers. Inasmuch as any drug studied in such centers must first have passed *exhaustive* preliminary laboratory studies, it is usually to the benefit of patients that they happen to be hospitalized in medical centers and can receive the latest advances in therapy. Patients who still feel that they are "guinea pigs" and object to receiving the latest advances should, of course, not be used for such studies. There is usually not enough of the new drug to go around anyway, and there will usually be plenty of patients who appreciate the opportunity to receive the latest in therapy.

Antihistamine Studies

Returning now to the matter of "double blindfold" studies, their importance can best be appreciated by considering a famous series of studies. In 1947 Brewster[4] published an article indicating the antihistaminic drug Benadryl was a useful therapeutic agent in the treatment of the common cold. Brewster tried the drug on 100 patients, used no controls, and issued a modest two-page report. It seemed to him that antihistamines were very useful in the treatment of the common cold, providing they were given early, but it certainly should be said to his credit that he appreciated the preliminary nature of his study and strongly urged further investigation before any firm conclusions were drawn. Brewster then studied 500 patients using codeine and papaverine as control drugs and after two years of investigation, produced the data[5] shown in the table at the bottom of the page.

Brewster also took into account the fact that a variable incidence of patients with real allergies might bias either the control or the treated group and therefore he ruled out all cases of allergic rhinitis as far as he could, and further controlled this matter by showing that a history of allergy was not more common in the treated group than in the control group. In 1949 the Food and Drug Administration released antihistamines for over-

PROPORTION OF PATIENTS WITH COLDS RELIEVED BY TREATMENT

Time of Onset of Treatment (Hours)	1	2	6	12
Patients treated with Control Drug	1/2 (50%)	1/2 (50%)	5/12 (42%)	7/22 (31%)
Patients treated with Antihistaminic Drug	19/21 (90%)	48/55 (87%)	116/156 (74%)	165/234 (70%)

the-counter sale and a period that has since been termed the "cold rush" began. The preparation Antihist is said to have been sold to the amount of one million dollars in one month. The total antihistaminic sales zoomed from two million dollars in 1947 to 35 million dollars in 1949[6]. Several other studies, including at least one in which a "single blindfold" procedure was used, the patient but not the physician being ignorant of the exact schedule of drugs, confirmed these data. Data from one of the other studies is shown below[7].

Mean Duration of Colds in Patients Receiving Various Treatments

Antihistaminic drug (26 patients)	Placebo 6.2 days	"Usual Treatment" (30 patients) 5.1 days
(40 patients) 1.2 days		

On the other hand, certain studies such as those of Lowell[8], the Naval Medical Research Unit Number Four[9], and the British Medical Research Council[10] did not confirm the above. The American Medical Association took a very dim view of the evidence favoring antihistaminics in the treatment of the common cold.

The general public, the Food and Drug Administration, and the drug houses have at least a partial excuse for accepting the claims for the antihistaminic drugs. The common cold has been estimated to cost the country about three billion dollars a year in lost time, medical care, etc., and it would hardly be expected that people would ignore the possibility of doing something about it at last. After all, there were certain data favoring antihistaminic treatment. However, the general public's misinformation was made much worse by certain writers in the lay press. These writers, with very little scientific basis, apparently judged studies by the number of patients in the study, more or less going on the assumption that a study involving 300 patients was automatically better than one involving 100 patients. The fallacy of this is obvious in view of what has been said above about the necessity of blindfolds and controls. Some fantastic logic was used by such writers and indeed, it appears that certain of them simply suppressed information that did not support their ideas. The American Medical Association was denounced, as usual, as the enemy of progress, etc., etc., etc. Although the press has in the past decade become a much more responsible organ in informing people about scientific advances, it is still unfortunately true that a certain number of writers who are not in the least qualified to consider drug evaluations write columns in which they turn medical discoveries into political weapons to lambast those whom they do not like. (This is, of course, also true for drugs other than antihistaminics. One of the most disgraceful attacks in recent years was that put forth by a very well-known columnist, highly regarded by many intelligent people who ought to know better. He completely ignored the very careful study done on a so-called anticancer drug, a study which showed it to have little or no value, and in a nationally syndicated column accused the physicians of attempting to murder important personages by withholding the benefits of this allegedly marvelous drug from them.)

The American Medical Association pointed out[11] that the mainstay of Brewster's conclusions in the above data is in the results in the two-hour group. If one takes the results at six hours and subtracts those at two hours one gets no significant difference between treated and controls. Therefore it behooves us to examine the two-hour group carefully and we see that there were only two controls in the two-hour patients. Indeed, even at six hours there were only 12 controls. In view of the possibility of errors in diagnosis, evaluation or even bookkeeping, it is obvious that a study of this importance should have more than two control patients in the significant categories. But this objection does not hold for the second set of data presented. These data were probably biased by the fact that the physician was not "blindfolded" and therefore, despite his best intentions, probably prejudiced. After all, it is very difficult to establish the exact time at which the common cold comes to an end. Even with the best intentions in the world, a physician is likely to be biased, at least unconsciously, in his interpretation unless he too is "blindfolded."

The atropine-like effect of certain antihistaminic drugs may have contributed to a certain degree of relief of symptoms of nasal stuffiness, etc. Therefore, a small genuine effect of antihistaminic drugs cannot be ruled out. On theoretical grounds there is no particular reason why antihistaminics should have a great effect against a disease thought to be viral in origin. However, if the studies had really been carried out with the proper technic and had still shown a striking and valid effect of antihistaminic drugs, then the theoretical grounds would simply have had to be reconsidered!

Random Selection of Patients

The matter of randomization in the selection of patients and controls has been mentioned briefly above. Drug A may give a falsely better result

than drug B if drug A is used in ambulatory patients, who are presumably less severely ill, while drug B is used on ward patients, who are usually sicker. A comparison of drug A versus drug B, using both ward and outpatients, would require that the distribution of both groups be the same for both drug A and drug B. Because of the fact that there may be many other variables which one may not appreciate, the safest course is always to allow for random selection of patients in each group. For example, it may be decided that the first patient meeting the necessary criteria who comes on the ward will be patient number 1, the next patient will be patient number 2, etc. Then from a table of random numbers one can decide which numbers indicate patients who are to receive the drug and which are to be controls. The method of numbering the patients originally can be varied to suit the circumstances, but the important thing is that the basis for giving the numbers to patients should be a predetermined one, in order to avoid selection that seems random but really is not. For example, if one reached into a group of charts and picked out ten, intending to make these patients the treated group, and then picked out another ten intending to make the second set the control group, one might get considerable bias. This is due to the fact that the older and more dog-eared charts might be the first ones that came to hand easily. These might be charts of patients whose cases were more chronic and therefore bias would be introduced[12]. It is usually possible to test, at least roughly, for the effectiveness of the randomizing procedure. If one sets up two groups, such characteristics as the incidence of various ages and the ratio of males to females would be expected to be approximately the same in the two groups. Stratified sampling can be used to make the comparison between various subgroups even better. Thus, in a comparison of drugs A and B in the treatment of tuberculosis, one might place the tuberculosis patients in several classes. Class I might consist of those with minimal, class 2 those with moderately advanced, and Class 3 those with far advanced lesions. There might be a separate class for those who previously had unsuccessful therapy with other drugs. Then within each of these classes, drugs A and B would be given on a random basis. Such stratified sampling is particularly helpful if one later intends to bring drug C into the trial because one can then get a class of patients for treatment with drug C with fair assurance that this class can be made quite similar to one of the subgroups treated with drugs A and B. Details of the differences in response to drugs in various subgroups, such as the success of the drug in the old versus the young, etc., also come to light more easily with stratified sampling. Furthermore, with stratified sampling it is not necessary to use simultaneously the treatments which are being compared. Thus one can use drug A in one year and then drug B in another and rely upon careful subdividing of the groups to make sure that the patients treated in one year are very similar to those treated in another year. This method of studying one drug during one period of time and another drug during a subsequent period is, however, very dangerous from the statistical standpoint, and may easily lead to false conclusions. For example, in comparing drug A with drug B in the treatment of angina pectoris, if drug A is given chiefly in the spring and summer while drug B is given during the colder season, drug A will probably give much better results than drug B for the simple reason that angina tends characteristically to be less troublesome in warm weather. In the previously noted Massachusetts General Hospital Study[2], the response of patients to a placebo was considerably different at two different periods of the year.

Variables

Sometimes it is highly desirable to do away with the problem of certain variables simply by eliminating them. Thus, if it is suspected that the presence or absence of liver disease will affect the treatment and there is reason to fear that patients with liver disease may not be distributed equally between treated and control groups, it may be decided in advance that no patient with liver disease will be used in a certain study at all. This may be all well and good, but there is the danger of making such a "superselection" that the results, though perfectly valid, have very little practical usefulness. For example, it may be established quite clearly that one drug is better than another in the treatment of white males between the ages of 15 and 20. But the population consists of many more people than white males between the ages of 15 and 20 and one is still left to wonder about the management of the population as a whole. Furthermore, the investigator must try to have some realistic appreciation of the importance of certain variables and the relative unimportance of certain others. It will never be possible to make a study so perfect that there are no differences between the treated and control groups except the treatment itself. There are always likely to be some minor differences in the characteristics of the two groups. It is important to insure that those differences which are allowed to creep in are relatively unimportant. For example, when Boyle established his famous physical law regard-

ing the effect of pressure on the volume of gases, he did not control the temperature very carefully. Now we know that differences in temperature do cause differences in volume and pressure of gases, and his experiment was to some degree in error in that he did not control temperature carefully enough. Nevertheless, Boyle had observed, as Conant[13] points out, that although there was some effect of temperature, the effect did not seem to be very great. Therefore, a variable which he did not control failed to ruin his experiment because the effect of the variable was not sufficiently great.

In a study comparing various doses of penicillin in the treatment of subacute bacterial endocarditis[14], stratified sampling was not used but the workers had the good sense to realize that differences in the sensitivity of the infecting organisms to penicillin might easily influence the results. Therefore, they checked on this point carefully and found that within a range of one to ten units of penicillin per milliliter the sensitivity of the organism did not affect the results. Having assured themselves on this point, they were able to ignore the factor of sensitivity differences within the aforementioned range and did not have to go to the great trouble of making the various treated and control groups exactly comparable in this respect.

It should not be assumed that the trial cannot show anything beyond the comparative percentage of cures or the comparative percentage of deaths in each group. In the trial of streptomycin in the treatment of tuberculosis conducted by the Veterans Administration and others, a great deal of information was gained as to the best schedule of streptomycin treatment, not only to produce satisfactory results from the cures, but also to produce satisfactory results from the standpoint of avoidance of serious toxicity. In other words, the physician may be concerned with a great deal more than simply answering the question: Is treatment A better than treatment B? He may wish to know for example, once treatment A has proved to be better than treatment B, whether or not he can rearrange treatment A in order to get the same good results with fewer side effects.

Use of Statistics

The use of statistics has been implied in a great deal of the above discussion. Statistics, however, will not save a trial which has been poorly designed from the outset. It is true that few if any trials can be perfectly designed from the outset, and it is usually necessary to modify the trial as one goes along, however undesirable this may be in theory, simply as a practical recognition of the course of events. For one thing, as indicated above, ethical considerations may make it necessary to remove a patient from the trial. (It is usually desirable to keep full protocols on such patients, even though they are removed from the trial, in order to get some indication as to how much the trial has been disturbed by removing the patient.) Nevertheless, many trials have probably been ruined because they were improperly planned from the start.

Additional information can be obtained from the use of statistics; for example, in an experimental design allowing every patient to serve as his own control, *i.e.* testing every patient both with the drug and without the drug, one may properly perform certain mathematical manipulations that may look at first glance like "cheating"[15]. These manipulations depend in essence on the following consideration: if the same patient receives each treatment, then one may find that whenever any patient experienced toxic effects after drug A, he always experienced toxic effects after drug B also, whereas several people who experienced toxic effects after drug B did not get them after drug A. Even though the differences in numbers may not be very impressive, a situation in which the difference in a patient's reaction to the drugs, if it occurs at all, always favors one of the drugs, is rather strong evidence that the favored drug really is less toxic. On the other hand, it is a well-known fact that a variety of false conclusions can be obtained from the improper use of statistics. For example, the commonly seen statement, "P equals .05," means that the probability that a difference at least as large as the one found could be due to chance alone is equal to 5 percent. It means similarly that the probability that such a difference is not due to chance alone, and was therefore a truly significant difference, is 95 percent. One can readily see that such a difference is probably significant. On the other hand, two treatments that really do not differ significantly may, one time in 20, happen to show a difference. Indeed, this is what one means by the statement, "P equals .05." If a large enough series of drugs, none of which really differs from another, is tested, there may be perhaps 20 different tests of one drug against another in the course of the whole study. It should therefore not be surprising if somewhere among those 20 tests, simply by the operation of chance, a difference occurs. The statement "P equals .05" would still hold true but the statement would now have little significance. Consider the question, "Is it difficult to roll double sixes with dice?" Obviously if there is to be only one throw of the dice, it is not com-

mon to throw double sixes; chance alone will let this happen only once in 36 times. If very many double sixes turn up on the first few throws of the dice, one begins to suspect that chance alone is not operating, *i.e.* that the dice are loaded. However, if the dice are to be thrown 40 or 50 times, it would not be surprising that once during that time double sixes would turn up. This would not necessarily indicate that the dice were loaded. Once the difficulty discussed above is recognized, the statistician can solve it with appropriate mathematical technics. The danger lies in failing to recognize the problem. (It may seem strange to the reader that successful treatment is compared to loaded dice; but it is plain that the aim of the physician is to see to it that the patient get a better "break" than would be allowed by chance alone. The aim of one who loads dice is also to see that he gets a better "break" than would be allowed by chance alone. The ethics of the two situations are considerably different, but in principle the physician with a useful drug is trying to do the same thing as the gambler is doing when he loads his dice; each is trying to see to it that the results are better than would be expected by chance alone.)

Need for Careful Studies

In conclusion, it should be stressed again that new drugs, before being put on the general market, should be studied very carefully, first in the laboratory and then, in gradually increasing doses, under hospital supervision. It is not safe to assume that a drug, chemically very similar to another drug of known usefulness, is itself safe to use. During World War II it became critically important to obtain new and better antimalarial drugs. Various chemical derivatives of the antimalarial drug pamaquine were studied. As minor chemical modifications of the drug were made, the known toxic effects of pamaquine were sometimes increased and sometimes decreased. However, in the midst of this series there occurred a compound that differed chemically only very slightly from the others in the test and yet when put into monkeys, caused fantastic toxic effects[16]. The new compound virtually destroyed the monkeys' central nervous systems. It is clear that it would have been a grave mistake to attempt to use this drug in patients. It is also clear that the antivivisectionists, who object to the use of laboratory animals, are maintaining an absurd position. For if we were to listen to them, we would be forced either to try drugs at the very beginning in human beings, with the possibilities of frightful reactions, or we would have to cease trying any new drugs at all, with a complete standstill of medical progress in drug therapy.

It is hoped that the above will convey some of the problems and some of the attempted solutions in the field of drug evaluation. Most important, it is hoped that the above has made clear the important role of the hospital medical center in this type of work and therefore the important role of pharmacists associated with such centers in preparing and supplying the necessary drugs and placebos. The fact that the dosage may vary as the trial progresses, that the form in which medication is given may also vary in different parts of the trial, make this type of work sometimes unusually difficult, and a considerable challenge to the pharmacists's skill and alertness. By the same token, this field gives the pharmacist a chance to make another really useful and significant contribution.

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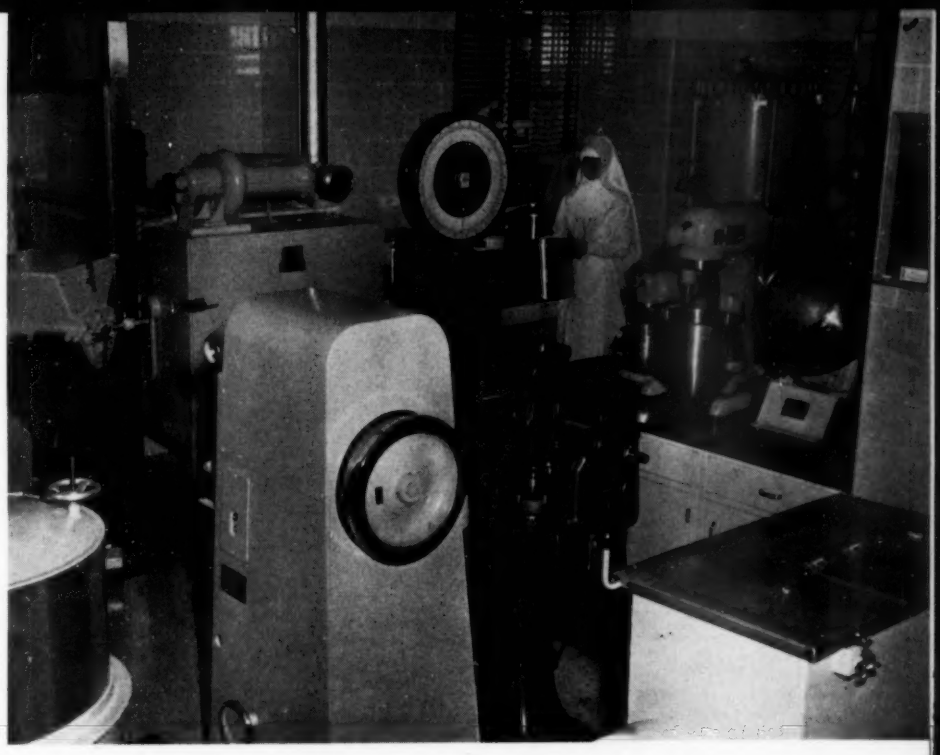
EFFICIENCY

in planning and maintaining the hospital pharmacy

by SISTER MARY BERENICE, S.S.M.

Sister Mary Berenice, S.S.M., Director of Pharmacy Service, at her desk in The Cardinal Glennon Memorial Hospital Pharmacy.



The tablet preparation room of the Cardinal Glennon Memorial Hospital Pharmacy.

IN SPEAKING OF EFFICIENCY in the hospital pharmacy, there can be no distinction made between the large and the small hospital. Regardless of the size of the pharmacy, it must be planned, developed, and maintained with efficiency. Size should have no adverse bearing on the efficiency of operation.

Efficiency is defined as "the ratio between the work accomplished and the amount of energy expended." Today, there are many men and women who make a profession of finding ways and means to accomplish more and more with the least possible expenditure of time and energy. We are all caught up in this movement with the efficiency experts, to a greater or lesser degree, depending upon our circumstances and individual abilities; the profession of pharmacy has joined this mighty upsurge of intense development.

Objectives and Policies

A fundamental adjunct to efficient hospital pharmacy operation is careful planning of the department. An adequate allotment of floor space is essential and must be supplemented by an arrangement that is properly organized and equipped to fill the needs for which the department is built. The time for making these plans is when the physical plant of the hospital is in the worksheet and blueprint stage. Fortunate is the pharmacist who has this opportunity, but he must be prepared to take advantage of it by knowing:

1. The objectives and policies of the hospital and the pharmacy.
2. The bed-capacity of the hospital and whether or not the plans include an outpatient department as well as the estimated daily visits, if such a department is in the specifications.
3. Whether the hospital service is to be general or specialized.

Along with this general information about the hospital, the pharmacist, in planning his department, should have a definite notion of the extent and scope of the activities to be carried on in the pharmacy itself. He should determine whether or not they will consist in:

1. Compounding and dispensing only, and if so, will this service be limited to inpatients, or also extended to outpatients.
2. Drug manufacturing of:
   a. Large volume of sterile solutions.
   b. Manufacture of nonsterile products in bulk.
   c. Small scale operation of only a few selected items.
3. Educational activities in which the pharmacy will engage, particularly internships or residencies in hospital pharmacy combined with graduate work, and the type of academic program involved of which there are a number of possible patterns, namely:
   a. One year of academic work and one year of practical education.

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A portion of the Inpatient Dispensary of the Cardinal Glennon Memorial Hospital Pharmacy.

b. Two years of part-time academic work and part-time practical education.

c. One semester of academic work, then two semesters of practical education followed by one semester of academic work

Each of these three programs requires a minimum of 1,920 hours of practical education, but 2,000 or more hours are preferred.

d. Hospital pharmacy internships not combined with graduate work.

e. Interdepartmental educational programs (student rotation through all departments and services of the hospital so that he may obtain a better knowledge and understanding of these areas, and of the relation of the Pharmacy to all these other departments and services).

f. Other intradepartmental educational programs.

g. Teaching of student nurses, interns, residents others interested in patient care.

It is only after careful consideration of the above factors, and the formulation of definite plans concerning them, that the pharmacist can determine the specifications for his department with regard to floor plans, equipment lists, etc.

Construction Costs

In the over-all planning of a hospital, it is estimated that 10 percent of the construction cost is equivalent to the cost of Type II equipment (movable equipment not included in the building contract) and Type III equipment (items such as graduates, spatulas, etc., which are requisitioned as needed).

Most likely the 10 percent estimate of construction cost would not apply to equipment for sterile and nonsterile manufacturing, if the pharmacy costs are considered separately. If, however, the construction and equipment costs of the pharmacy are to be included in the total cost of the entire hospital, it is probable that the 10 percent estimate would then apply. A practical example of this was demonstrated in the planning and building of the Cardinal Glennon Memorial Hospital for Children, which was opened in July of this year. The entire cost of the hospital was based on the cost per square foot, and the cost of the pharmacy area was allocated to that department.

In this computation, the 10 percent estimate of the construction cost was far below the cost of the pharmacy equipment; in fact, the cost of equipment was approximately 90 percent of the construction cost of the pharmacy area. But when the cost of the construction of the pharmacy area and the equipment cost was included in the cost of the entire hospital, the total cost of all Types II and III equipment did equal 10 percent of the total cost of construction for the hospital. The construction costs of hospitals, including Type I equipment, today varies between $18 and $25 per square foot. Construction costs, which include Types II and III equipment, may range from $20 to $30 per square foot. The cost per hospital bed may average between $20,000 and $30,000.

The foregoing leads one to conclude that the Pharmacy Department, where bulk manufacturing is to be undertaken, represents a considerable investment. Before beginning such an enterprise there must be reasonable assurance that the undertaking is sound, practical, and that the program can be carried out successfully.

Size of Pharmacy

A number of accepted methods for determining the size of a hospital pharmacy are estimates based on the number of beds in the institution. Some use the figure of five square feet per hospital bed, if the bed capacity is 200 or more; in larger hospitals (over 500 beds) the ratio can be less; and in the very small hospital the ratio should be greater.

The sterile solution room at the Cardinal Glennon Memorial Hospital Pharmacy.

It may be well to pause here and consider an important phase of hospital planning which seems to be pertinent to this discussion. It is far easier and much less costly to add more beds, as the need arises in a hospital, than it is to enlarge the area of one of the special departments. As the size of the hospital is increased, the work-load of all the services increases and, unless cognizance is taken of this fact in the original planning, subsequent enlargement of the special departments to meet the added needs is impossible without considerable waste of present facilities. A forward-looking building program, based on prudent planning and foresight, will carry specifications that allow a larger area than seems to be adequate for the existing needs for not only the Pharmacy, but all of the special departments. Many present-day hospitals have outgrown their facilities and there are many hemmed in so that expansion is impossible; if remodeling is required in moving one of these departments, it is both time-consuming and costly. Estimates show that it is much simpler and less costly, as well as more efficient, to add more floor space for beds than it is to attempt to move a special department to another site.

If the hospital is to include an outpatient department, it is estimated that one pharmacist is required for each 100 prescriptions filled per day, and one pharmacist is required for each 100 hospital beds. This consideration is pertinent in the planning stage of the pharmacy in order that the work-area for each pharmacist will be adequate.

The bulk manufacture of nonsterile products requires another four square feet per hospital bed, and the manufacture of sterile products will require an additional four square feet per hospital bed. Of course, these are merely estimates, not requirements. The estimates must be applied to the existing needs in the specific situation. The sterile manufacturing section should have three divisions: one for the clean-up area, the second for the preparation of solutions, and the third for sterilization. A quarantine area should also be provided where the sterile products are kept until all sterility, chemical, and pyrogen tests have been completed. As was stated before, much careful study and planning is necessary to achieve the most economical arrangement and utilization of the area allotted to the department.

Equipment for Manufacturing

The second basic consideration in the planning stage of the Pharmacy is the equipment and mechanical apparatus to be used in carrying out the pharmacy program. There must be assurance that the equipment will produce the type of products desired. A hospital pharmacy should never manufacture just for the sake of manufacturing. There must be a definite purpose in the choice of products to be manufactured, based on the following production guides:

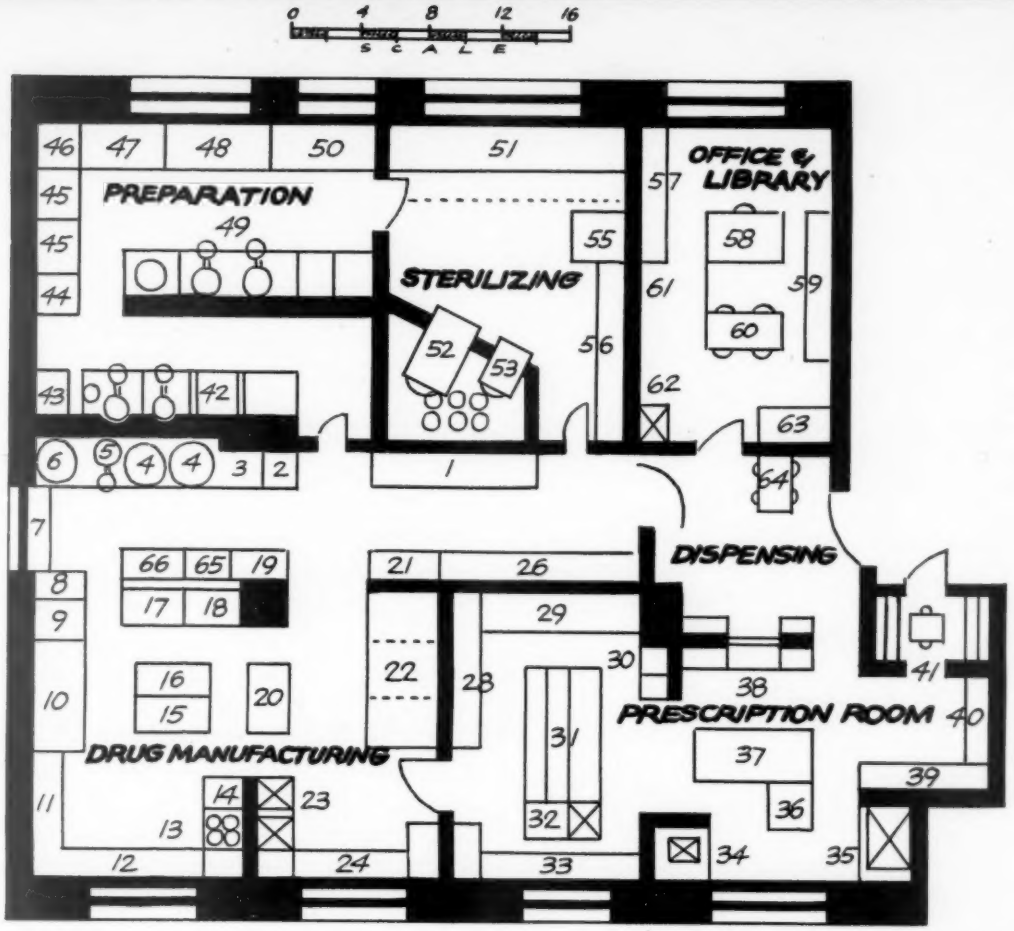
1. The products to be made are needed and are not on the market.
2. The products can be manufactured by the Pharmacy at a lower cost than the current market price for the finished products.
3. The manufacturing program is to be used as an educational device.

Initiating a manufacturing program involves many problems. When the sterile solutions room at Cardinal Glennon Memorial Hospital for Children was still in the planning stage, we were confident that the production of sterile solutions for our 1,200 hospital beds would begin as soon as the hospital opened. Almost everyone we consulted about the project, during the early planning period said, "Why, there's just nothing to it! The stills are equipped with purity meters, and if accuracy is employed in their preparation, there will be the assurance of good solutions; good technique secures protection from pyrogens, so there is no reason why the end results should not be good solutions." However, it was not quite that simple. The number of problems which presented themselves, at the outset, was surprising, indeed, and it seemed that each had to be solved, individually.

In manufacturing parenteral fluids, the pharmacist cannot be satisfied with solutions that are "just good enough"—he must have certain proof of the excellence of these preparations. They must pass the sterility, chemical, and pyrogen tests before they are released for use. Permanent records of each batch of sterile solutions or other sterile products, as well as of the nonsterile products, are to be kept so that these records are always available to certify the quality of the products manufactured.

The degree of excellence of the manufactured products will depend, of course, upon the quality of equipment and supplies to be used in the process of manufacturing. But more important than this is the efficiency and accuracy in technique. The pharmacist must be firmly convinced that anything short of perfect products is just not "good enough."

As was mentioned before, it is necessary to determine which preparations can be manufactured, routinely, with profit; the amount expected to be used over a certain period of time, and the method to be employed in making these products. These determinants influence the choice of equipment. Equipment selection is part of the



Floor Plan for Pharmacy Department, Cardinal Glennon Memorial Hospital for Children

Manufacturing Room

1. Cabinet
2. Colloid Mill
3. Filter Press
4. Mixing Tanks
5. Still
6. Storage Tank
7. Table, Paper Racks
8. Toledo Scales
9. Drying Oven
10. Hood, Granulater Mixer
11. Work Top, Cabinet below
12. Work Top, Wide Carriage Typewriter—Cabinets below
13. Electric Stove
14. Bottle Washer
15. Tablet Punch
16. Oint. Tube Filler and Crimper
17. Hobart Mixers (2)
18. Tablet coater & Polisher
19. Ointment Mill
20. Tablet Granulator
21. Enclosed Gramatic Balance
22. Refrigerator
23. Sink
24. Work Top, Cabinets below
25. & 26. Cabinets
26. a. Change Can Mixer
    b. Age Mixer

Prescription Room

27-28-29-30 Cabinets
31. Double Prescription Counter
32. Sink
33. Work Top
34 & 35 Dumb waiters
36. Typewriter & Table
37. Dispersion Table
38. Prescription Counter
39 & 40 Files

Night Emergency (Daytime use - to see salesmen)

41. Cabinets, Table, two chairs

Sterile Solutions Room

42. Clean-up area
43. Flask washer
44. Ampul washer
45. Work top, Purdum-Gregorek Soluter

46-47-48 Work tops, Solution Mixing Tank and carts below

49. I.V. Preparation, Concentr. Bottle & mixing unit—10 gal. hr. stills, Recording Conductivity meter (all stills are thus equipped)
50. Cabinets
51. Sterile Loading & Transfer carrier & Flask drain carrage
52 & 53 Sterilizers
54. Deionizers
55. Dry Sterilizer
56. Cabinets, quarantine area

Library and Office

57. Files
58. Desk & Chair
59 & 63 Bookcases
60. Table & chairs
61. Typewriter & table
62. Sink

Pharmacy Lobby

64. Reading area—table & chairs

PHARMACY DEPARTMENT AREA

	Square Feet
Prescription Room	546
Night Emergency Room	35
Office and Library	198
Pharmacy Lobby	138
Non-Sterile Manufacturing	686
Sterile Manufacturing	495
Storage Area (2 floors below Pharmacy—connected by dumbwaiter)	1,588
TOTAL PHARMACY AREA	3,686

early planning because it is necessary to know exactly how much floor space the equipment will occupy when installed. These measurements must then be fitted into the blueprints of the department, to make sure that a place is provided for every piece of necessary equipment; that there is adequate allowance for the work area; that the arrangement is economical of time and motion; and, finally, that no floor space is wasted. It is also necessary to secure mechanical drawings of each piece of equipment in order to determine the roughing-in dimensions, outlets, connections, floor drains, and the voltage on all electrical equipment. Directions for installation also should be obtained in advance from the manufacturers of the equipment.

Work Flow

Another important point to be borne in mind, when planning a pharmacy, is that the inter- and intra-departmental work-flow must also receive careful preliminary consideration. This is essential to the proper placement of mechanical apparatus and other equipment; for instance, there is an advantage in the proper placement of dumbwaiters. And, speaking of dumbwaiters, these appliances can be obtained with a wide variety in types of control. This is a significant fact because it is possible to have dumbwaiters installed which will not serve the purpose for which they are intended, simply because the controls are not the right kind.

Metal storage cabinets are also an important pharmacy item. Many variations are available in the grade and finish of the metal. If the cabinets are enamel, it is well to specify "baked enamel" because the sprayed and air dried enamel will not stand the wear and tear of daily routine; this type will present a constant housekeeping problem, because the finish tends to chip and renovation is hardly possible because a new coat of finish is just as wear-sensitive as the first. The doors of metal cabinets ought to be insulated with cork to eliminate noisy opening and closing. It is also well to keep in mind that not all grades of steel are rust-proof.

The statement that "your education is just beginning the day you get your diploma" could never be applied more fittingly than to the present-day hospital pharmacist. Countless opportunities of continued growth and education are offered in this field. Part of the obligation of the hospital pharmacist is to keep abreast of current discoveries and developments in his profession. Since it is a physical impossibility for the individual to read and digest everything that is published in the trade journals, a schedule of pharmacy staff meetings—once or twice a week—provides an excellent means for the exchange of ideas through reports; panel discussions and seminars, in which every staff member participates so that all may benefit by the knowledge of the others. Mimeographed copies of the summaries or condensations of these reports are made available to all members of the staff.

To initiate and conduct an internship program in hospital pharmacy is another excellent means of progressing in the field of hospital pharmacy. This type of activity is both a challenge and a stimulus to keep abreast of developments in the field.

It is easy to recognize the many advantages there are in being able to plan the Pharmacy Department at the time the hospital building is erected, but there are also some points in favor of having an established department in which additional equipment is procured as the need arises. Sometimes it is not possible to initiate full production in the Pharmacy at the time the hospital is opened, if the department is fully completed. Nevertheless, if a choice could be made, most pharmacists would probably choose the completed department. But in reality no department is ever fully completed; there must be a continued development—day by day and year by year—because progress in modern research does not stand still but ever reaches out to wider and wider horizons.

Stock Control

Of necessity, the modern hospital pharmacist must concern himself with efficiency in all pharmacy operations such as the evaluation, selection, control and storage of drugs, and the application of good business principles with regard to all transactions: purchases, requisitions, inventory, etc.

One of the most effective tools in maintaining stock control is the perpetual and the physical inventory. Physical inventory should be taken, at least once a year, and then checked against the perpetual inventory. With regard to items purchased in small quantities, it is not necessary to make deductions each time a small amount is used, but the item should be considered used and checked off the inventory record when the supply is low enough to re-order. Another phase of stock control is the checking of drugs in stock on the nursing division. Such a periodic check is necessary so that an excessive amount of drugs will not accumulate in these areas, and so that discontinued drugs will be returned to the pharmacy.

Sound business principles indicate that money

invested in drug supplies should have a turnover four or five times yearly. A rate of less than four may be indicative of overstocking, while a turnover of over five shows that some items will be out of stock when they are needed. Both these situations militate against efficient service. Efforts should be directed toward keeping the inventory as low as possible, but within the limits set by principles of management concerning good buying and prompt, efficient service.

An important aid in keeping the stock properly rotated, so that the older stock is used first, is the marking of all items at the time of receipt with their price and the date of purchase. This is also a safeguard against overstocking.

The arrangement of a definite pricing schedule makes for consistency in pricing and is also a basis for justifying any charges that are made. More than the figure appearing on the invoice for drugs must be taken into account in arranging a pricing schedule.

Factors Included in Costs

The following are some of the definite though not always obvious costs which must be included in the total cost of every item, whether purchased or manufactured, that is dispensed by the Pharmacy:

1. Heat, light, and power (computed on the basis of square footage).
2. Maintenance and repairs in the Pharmacy Department (a direct cost).
3. The pharmacy's portion of the general maintenance cost of the hospital (based on area allotment).
4. Dietary (cost per meal for those employees entitled to receive meals).
5. Laundry (cost per pound of soiled linens used in the pharmacy).
6. Medical records (percentage of cost allocated to Pharmacy).
7. Motor service (if such exists).
8. Housekeeping in the pharmacy (direct cost).
9. Housekeeping in the entire institution (percentage cost to the pharmacy).
10. The Pharmacy's share in the over-all administration cost.
11. Amortization of borrowed funds or perhaps of a lease; interest on borrowed funds and possibly rent charges.
12. Depreciation on building and equipment.
    a. Construction costs based on a 50-year life and charged each month as 1/12 of 1/50 of cost. (In a new building, it will most likely be possible to obtain the actual construction cost of the pharmacy area).
    b. Equipment considered as having a 10-year life; each month a charge of 1/12 of 1/10 of the cost of the equipment is made.
13. Electricity and water, as a direct charge or on some other basis.
14. Salary for all pharmacy personnel.
15. Possibly other obscure costs.

Pharmacy bookkeeping cannot be otherwise than in accordance with recognized business methods.

Work Schedules

The systematizing of departmental routine so that adequate pharmacy service is given, not only during regular hours but also at times when the Pharmacy is closed, is essential. This includes the handling of emergency calls with dispatch so that the best interests of the patient and the hospital are served; and planning on-duty schedules and work-loads so that they conform with the regular working hours, which means keeping overtime down to a minimum or curtailing it altogether.

Added to the duties already enumerated, the efficient hospital pharmacist must also devote considerable time to:

1. The preparation of sterile and nonsterile medications, either on a small or a large scale. The pharmacist, who was trained in a manufacturing department equipped with modern appliances, should be able to adapt himself to small-scale operation, with make-shift facilities; it is likely that more often than not he will be expected to work under some limitations.
2. The formulation and research in production and other related areas.
3. The dissemination of literature on recent drugs and drug therapy trends, as well as other information to physicians, medical and dental students and other professional workers concerned with patient care.
4. Making available his services to physicians in their research on experimental drugs.
5. Coordination of intra- and inter-departmental relations so that, through the pharmacist's interest and cooperation, others may benefit from his knowledge and experience.

The foregoing remarks have demonstrated the indispensable part which efficiency plays in the daily routine of the hospital pharmacy. It must be embodied in our policies and regulations both in short and long range planning. It must permeate every function of the pharmacy staff in their relationships and contacts with others. It must be the ever-glowing spark that fires our ambitions and spurs us on to our goal of prompt, generous service to the patients, our co-workers, and the hospital. And though our efforts are never quite as successful as we would like, we do not become disheartened because we know that our striving for 100 percent efficiency is just another phase of our striving for the "ever ancient, ever new perfection," of which St. Augustine so beautifully wrote, when he said: "Our hearts are ever restless until they rest in Thee (God)."

pharmacy apprentices

a source of new personnel for hospital pharmacy

by M. PIKE

WITH THE INCREASED NUMBER of hospitals in our country during the past decade has come a greater demand for qualified hospital pharmacists. The shortage of trained young pharmacists has been acute, as the number of graduates is limited, and most of these enter retail practice. All pharmacy graduates during their student days master the study of pharmacy, pharmacology, toxicology, chemistry and biology, etc. and it is this knowledge which equips them to become good hospital pharmacists. Why then do the vast majority of graduates end up in "the corner drug store"? As Chief Pharmacist in a general hospital, I am concerned with the lack of well educated and trained pharmacy personnel. I believe that the lack of interest in hospital pharmacy on the part of pharmacy students is due in part to ignorance as to the truly satisfying and

M. PIKE is Chief Pharmacist at the Long Island Jewish Hospital, Long Island, New York.

stimulating professional careers that are possible in our hospitals. The average pharmacy school gives the student little instruction in specialized phases of pharmacy practice, with the assumption that the student will enter the retail pharmacy field. Since we hospital pharmacists are ever faced with the problem of recruiting "new blood," we must utilize the best means at our disposal to educate and attract pharmacy students in this phase of the profession.

An internship program, as outlined by the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS can help alleviate the shortage by further training of students already interested in being hospital pharmacists. The group that requests internships are those who have already made their decision without guidance or experience in hospital work. However, it is my belief that we in hospital pharmacy should take additional steps to encourage pharmacy students to enter our specialty of practice.

Third Year Student

It is my feeling that the undergraduate third year student is the best person to approach. The student who has completed his junior year has had enough pharmacy, chemistry, and physiology to be able to profit by exposure to the practical phases of hospital pharmacy, and he is ready for instruction in pharmacology. If, through an apprentice system, the entire picture of hospital pharmacy were to be presented to the third year student, I am certain that more of them would be attracted ultimately to this practice of pharmacy. It is in hospital pharmacy practice that the pharmacist can most fully utilize all of his scientific knowledge on a daily basis. This fact will become evident to the student before he has committed himself to his future field of activity—before the commercial pharmacy has irrevocably claimed him.

With these thoughts in mind we, at Long Island Jewish Hospital, recently selected a third year pharmacy student who had requested a summer apprenticeship in hospital pharmacy. He was engaged for three months at a modest salary. After one month of experience under direct supervision he rotated as a vacation relief employee through all the jobs in the Pharmacy. His interest in the work and his enthusiastic performance of his duties more than convinced us of the correctness of this apprenticeship program. The instruction he received covered all phases of hospital pharmacy practice.

The following is a resume of the activities in which he was involved, an experience which both he and we are convinced has not only acquainted him with hospital pharmacy practice, but also stimulated his interest and desire to pursue a career in which his scientific training can be of greater use and provide more professional rewards. We believe a well organized formal program of hospital apprenticeship should be organized for all third year students. A greater number will go on to internship and employment in hospitals as a result.

Storage, Receiving and Distribution

During the first week the student assisted the pharmacy helper in receiving and storing of stock from suppliers. He also took part in delivering materials to all parts of the hospital. He received instruction in the handling of our perpetual inventory system. During this week the student became acquainted with the location of the various nursing and service units. When the helper was on vacation, the student performed all of his duties and kept the supply channels open.

Manufacturing

The second week of apprenticeship found the student assisting the helper in the preparation of bulk external solutions such as dilute alcohol, rubbing compound, mouthwashes, antiseptic solutions, cold sterilization preparations, and all other external liquids supplied to the various sections of the hospital. The student was also assigned to the preparation of bulk quantities of ointments. By the end of the fourth week he was preparing, under supervision, all the preparations, external and internal, which the Pharmacy normally manufactured.

Dispensing and Compounding

After one month, under the personal supervision of a registered pharmacist, the student was advanced to the prescription counter. At first he filled prescriptions for external materials. As he showed an ability to read prescriptions, calculate, interpret directions, check for overdosages and incompatibility, he started to fill all types of prescriptions, always checking with one of the registered pharmacists before filling. If the prescriptions were in any way unusual, as far as dose, calculation, combination, newness of drug, or errors in writing, these points were discussed with him.

Intravenous Solution Manufacture

Since our pharmacy manufactures most of the intravenous solutions used in the hospital, the student spent several days with the solution technician. This technician showed him all phases of

parenteral solution manufacture, and the apprentice assisted in the making of some of these solutions. The Pharmacy also produces smaller vials of injectable material, and the student also assisted in this manufacturing process.

Pharmacy Administration

The student was shown the various forms involved in the ordering of materials for the use in the various sections of the hospital. Narcotic controls were explained to him along with alcohol control. All necessary records kept for narcotics and alcohol, including monthly and annual reports were discussed. The pharmacy monthly report was explained, and he actually made up one of these. The student was also involved in the preparation and typing of various memoranda and directives to almost all departments in the hospital, and was given a good picture of the interaction of the pharmacy with all sections of the hospital. He was shown all phases of ordering and purchasing, including the visit by the detail men.

The student accompanied the Chief Pharmacist on regular inspection rounds to check overstocking, proper storage, outdated biologicals, and insufficient supplies at nursing units. He assisted with narcotic checking too. He was present at brief nurses conferences which dealt with problems of fluidity of distribution, new stock requirements, and improvement in dispensing directly to the patient.

Conferences and Demonstrations

Since at medical conferences drug therapy is discussed in a clinical context and with the patients full medical history as background, it was considered worthwhile for the student to sit in on at least one conference of each medical service in the hospital. Here, as a result, he was able to better appreciate the action of drugs on the human body, and hear the medical pros and cons for the use of many therapeutic agents.

The toxicology of many drugs was also discussed. After each medical conference, the Chief Pharmacist held a discussion with the student expanding on those points of pharmacology and pharmacy which were important or noteworthy.

In addition, the student spent one day in the Operating Room, the Morgue, the Anesthesia Department, and the Delivery Room. While procedures were in progress he received instruction from physicians in the action of the drugs being administered. The most important of these demonstrations was the process of anesthesia, for here he saw the immediate effect of potent drugs.

Educational Programs

The student was present at lectures in pharmacology that the Chief Pharmacist delivered to the nursing and pharmacy staff, and freely joined in the question periods.

Research Program

The student assisted the Chief Pharmacist as a technical assistant in some of the research work being done in the department. All of this work involved the use of animals, and the student learned some of the rudiments of animal investigation as a pharmacological tool. Needless to say he was most interested in that phase of his apprenticeship.

Formulary

The formulary method of control and dispensing was explained to the student and he actually participated in some phases of the revision of the present formulary.

It is quite evident that our student had a thorough introduction to hospital pharmacology. Here is a statement which he prepared summarizing his stay with us.

Statement:

I cannot stress too highly the value of serving some apprenticeship time in hospital pharmacy. I found that my theoretical knowledge of pharmacology and pharmacy was greatly enlarged, due to attendance at medical conferences and pharmacy lectures in pharmacology. Through discussions with the medical and laboratory staff, on a daily basis, a tremendous amount of knowledge was made available to me concerning the relationship of diagnosis to drug therapy. Hospital pharmacy deals with dosage forms which are rarely used in retail outlets, *i.e.*, ampuls, special formulae.

Hospital pharmacy affords an opportunity to gain experience in volume purchasing and dispensing rarely afforded in retail shops. Due to the formulary system, one quickly learns the generic nomenclature of all drugs and the composition of brand named items.

My visits to the Operating Room, Recovery Room, Anesthesia, and other units gave me an excellent opportunity to observe the action and effect of drugs given to patients. My frequent discussions with specialists in all phases of drug therapy did much to stimulate an interest in pharmacology.

I, therefore, feel that the student seeking a complete apprenticeship should spend some time in a hospital pharmacy, as it affords him the opportunity to see the practice of pharmacy entirely different than the retail. In the hospital one gets a good idea of pharmacy research, education, manufacturing, economics, and pharmacology. For those students who are not interested in the retail practice of pharmacy, hospital pharmacy offers a highly educational and truly professional pursuit of pharmacy.

POISON CONTROL CENTERS

ARIZONA, Phoenix
Paul B. Jarrett, M.D., *Chairman*, Committee on Safety, Maricopa County Medical Society, 2025 North Central Avenue, Phoenix, Arizona

DISTRICT OF COLUMBIA, Washington
Allan B. Coleman, M.D., 1433 Whittier Street, N.W., Washington, D.C.

FLORIDA* (Poisoning Control Program)

Daytona Beach
Joel V. McCall, Jr., M.D., Halifax District Hospital

Fort Lauderdale
John S. Fifer, M.D., North Brcward General Hospital

Fort Myers
A. Louis Girardin, Jr., M.D., Lee County Hospital

Gainesville
William Hadley, M.D., Alachua General Hospital

Jacksonville
J. K. David, Jr., M.D., St. Vincent's Hospital

Lakeland
Walter Price, M.D., Morrell Memorial Hospital

Miami
George Lister, M.D., Jackson Memorial Hospital

Ocala
Harry M. Edwards, M.D., Munroe Memorial Hospital

Orlando
Charlotte Maguire, M.D., Orange Memorial Hospital

Panama City
John J. Benton, M.D., Memorial Hospital of Bay County

Pensacola
Frank L. DeBusk, M.D., Baptist Hospital

Sarasota
Harry G. Morton, M.D., Sarasota Memorial Hospital

Tallahassee
George S. Palmer, M.D., Tallahassee Memorial Hospital

Tampa
James M. San, M.D., Tampa Municipal Hospital

West Palm Beach
Lawrence R. Leviton, M.D., Good Samaritan Hospital

ILLINOIS, Chicago
Joseph Christian, M.D., *Chairman*, Department of Pediatrics, Stritch School of Medicine, 706 South Wolcott Street, Chicago

ILLINOIS, Springfield
J. Keller Mack, M.D., St. John's Hospital, Springfield, Illinois

INDIANA, Indianapolis
Irving Rosenbaum, M.D., 401 East 34th Street, Indianapolis 5, Indiana, in association with Health and Hospital Corporation of Marion County, 307 City Hall, Indianapolis 4, Indiana

KENTUCKY, Louisville
William Curtis Adams, M.D., Assistant Professor of Child Health, Coordinator of the Louisville Poisoning Control Program, School of Medicine, University of Louisville, Louisville 2, Kentucky

MARYLAND, Baltimore
Maryland Chapter American Academy of Pediatrics
a) University of Maryland Hospital, Poison Control Center (24 hour service), Telephone: LExington 9-0320, Department of Pediatrics, Samuel Bessman, M.D., Associate Professor of Pediatrics, Poison Control Coordinator
b) Johns Hopkins Hospital - Poison Control Center, Telephone: ORleans 5-5500 (24 hour service), Department of Pediatrics, Thomas E. Reichelderfer, M.D., Instructor of Pediatrics, Poison Control Coordinator

MASSACHUSETTS, Boston
Lendon Snedeker, M.D., Executive Secretary, Boston Committee for the Control of Accidental Poisoning in Children, 300 Longwood Avenue, Boston 15, Massachusetts

MASSACHUSETTS, New Bedford
George W. Starbuck, M.D., Chairman, Accident Prevention Committee, American Academy of Pediatrics, 68 Arnold Street, New Bedford, Massachusetts

MICHIGAN, Grand Rapids
Mark W. Dick, M.D., 1508 The McKay Tower, Grand Rapids, Michigan

NEW JERSEY, Atlantic City
Samuel C. Southard, M.D., Supervising Director, Atlantic City Hospital, Poison Control Center, 26 S. Ohio Avenue, Atlantic City, New Jersey

NEW JERSEY, Newark
William W. Fost, M.D., Babies Hospital, 15 Roseville Avenue, Newark 7, New Jersey

NEW YORK, New York
Harold Jacobziner, M.D., Assistant Commissioner, New York City, Department of Health, 125 Worth Street, New York 13, New York

NORTH CAROLINA, Durham
Jav Arena, M.D., Duke Hospital, Durham, North Carolina

OKLAHOMA, Oklahoma City
H. A. Shoemaker, Ph.D., Director, Oklahoma Poison Control Center, University of Oklahoma Medical Center, 800 Northeast 13th Street, Oklahoma City 4, Oklahoma

PENNSYLVANIA, Harrisburg
Rosemarie J. Tursky, Child Health Committee, Dauphin County Medical Society, 1000 N. 2nd Street, Harrisburg, Pennsylvania

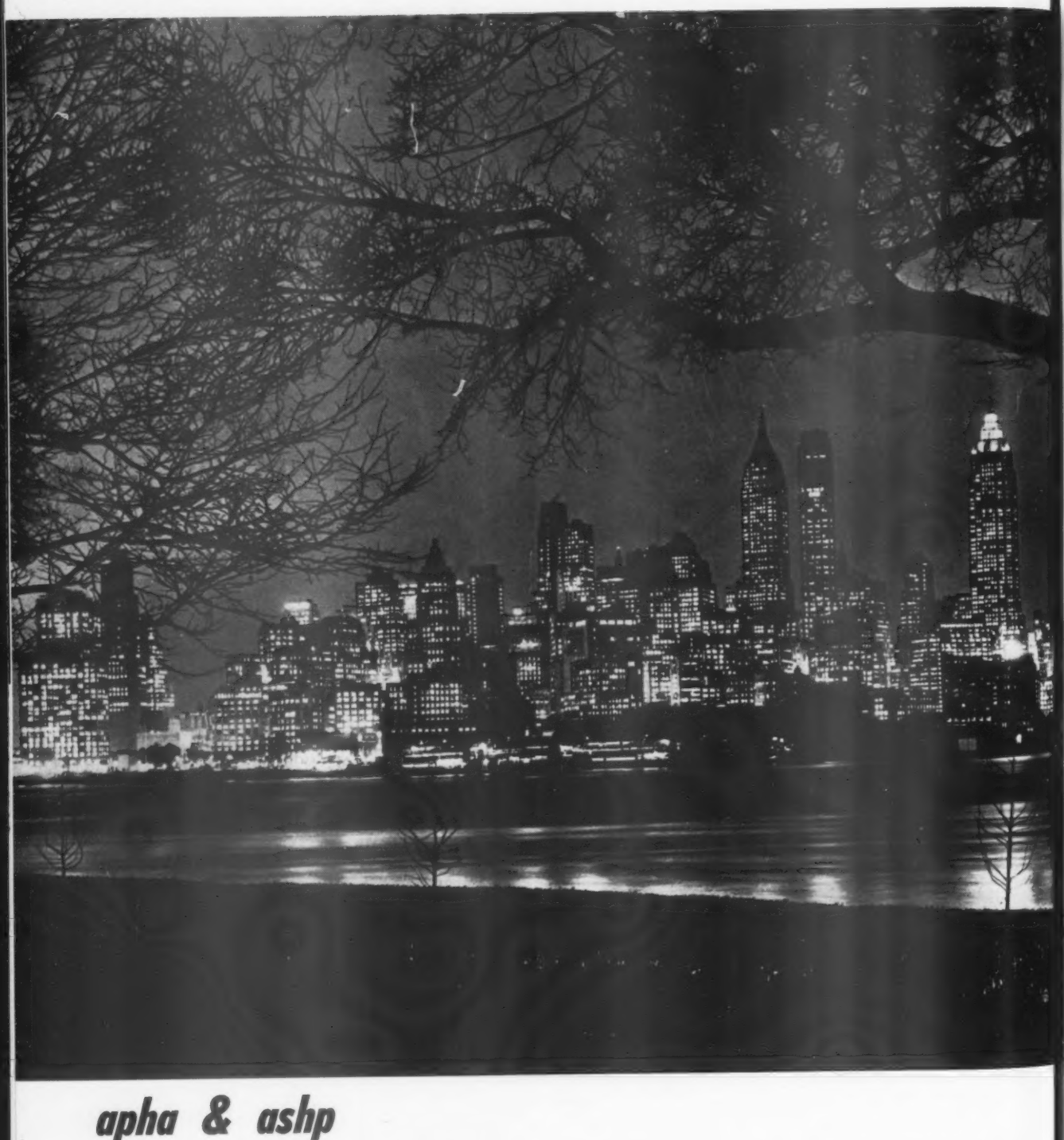
TENNESSEE, Memphis
Albert M. Jones, M.D., Poison Information Center, Le Bonheur Children's Hospital, Memphis, Tennessee

WASHINGTON, Seattle
Robert W. Deisher, M.D., Director, Child Health Center, University of Washington, Seattle, Washington, Committee Chairman, King County Hospital and Children's Orthopedic Hospital

WISCONSIN, Milwaukee
James O. Kelley, Executive Secretary, Medical Society of Milwaukee County, 208 East Wisconsin Avenue, Milwaukee, Wisconsin

*Established by the Florida Chapter of the American Academy of Pediatrics and the Florida Pediatric Society - 1956

NEW YORK CONVENTION



apha & ashp

APRIL 28 - MAY 3

New York City will be the site for the 1957 Annual Meeting of the American Society of Hospital Pharmacists which will be held in conjunction with the Convention of the American Pharmaceutical Association. During the week of April 28, members of the A.Ph.A. and affiliated organizations will meet at the Hotel Statler. The American Society of Hospital Pharmacists will convene on Sunday, Monday and Tuesday, April 28, 29 and 30, for its Fifteenth Annual Meeting. Since a great number of hospital pharmacists are located in the New York Area, a record attendance is anticipated. Also, representatives of the Society's forty-six affiliated chapters scattered throughout the nation will participate. A committee of hospital pharmacists headed by Miss Anna Grosso, Chief Pharmacist at Presbyterian Hospital in New York City, will act as host to members of the Society. Other members of the Local Hospital Pharmacy Committee include the following: Norman Baker, The New York Hospital; Leo Blackman, Mt. Sinai Hospital; Sister Mary Etheldreda, St. Mary's Hospital, Brooklyn; Sister Marie Patrick, St. Vincent's Hospital; Robert Bogash, Lenox Hill Hospital; Abraham Zarro, Manhattan General Hospital; and Sister Mary Jeanette, Mary Immaculate pital; and Joseph Messina, Memorial Center for Cancer Diseases.

Business Sessions

In addition to the presentation of papers and entertainment, which is scheduled during the Annual Meeting, the business of the Society will be transacted during the three day session. The House of Delegates, which includes representatives of the affiliated chapters, the members of the Executive Committee and the Chairmen of the Special Committees, will meet on Sunday afternoon at 2 P.M. The Address of the President-Elect, Leo F. Godley, will be presented at that time. Also scheduled for the House of Delegates meeting is the report on the American Formulary Service by Dr. William Heller, Chairman of the Committee on Pharmacy and Pharmaceuticals and a report on the Audit of Pharmaceutical Service in Hospitals by Don E. Francke, Principal Investigator for the study. Other papers to be presented at the meeting of the House of Delegates include the following:

"A Survey of Pharmacy Practices in Forty Smaller Hospitals," by Daniel F. Moravec, Director of Pharmacy Service, Lincoln General Hospital, Lincoln, Nebr.

"The American Hospital Association and Hospital Pharmacy," by Joseph A. Oddis, Staff Representative, American Hospital Association, Chicago, Ill.

The Executive Committee is giving considerable thought to the work of the House of Delegates and every effort is being made to better inform the representatives of the affiliated chapters regarding activities of the Society. Delegates should in turn be informed regarding the work of their local groups and be ready to present recommendations or problems for discussion at the Sunday afternoon meeting of the House of Delegates.

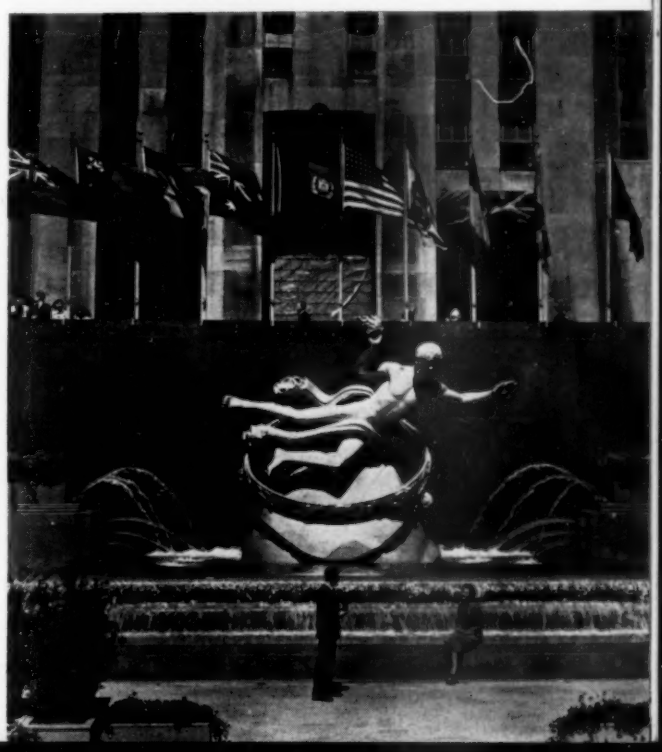
The reports of officers and committee chairmen will be covered throughout the two day meeting. The Society's Executive Committee will meet on Saturday, April 27. Any matters which should be called to the attention of this group should be in the hands of the Secretary not later than April 5.

Every chapter is urged to name a delegate and make definite plans to have representation at the meeting. All committee reports will be available in mimeographed form and will be published in full in the July-August issue of The Bulletin, so that the membership as a whole will receive detailed reports.

Entertainment

Another highlight of the 1957 Annual Meeting will be presentation of the H.A.K. Whitney Lecture Award at a dinner scheduled on Monday evening at the Hotel Statler. This Award was established by the Michigan Society of Hospital Pharmacists in honor of Mr. H.A.K. Whitney, first Chairman of the Society. It is given annually to an individual who has made outstanding contributions in the field of hospital pharmacy. Although traditionally the award has been presented

Statue in Rockefeller Center



at a local meeting of the Michigan Society, it was agreed to hold this event at the Annual Meeting this year. This decision came about as the result of the success of the 1956 Whitney Award dinner, which was held in conjunction with the 1956 Annual Meeting in Detroit.

Also, the traditional breakfast for hospital pharmacists is scheduled for Tuesday morning. Tentative plans for entertainment are being made by the local committee and will be announced in a letter to all members of the SOCIETY.

The ASHP will maintain a suite of rooms where hospital pharmacists may meet informally throughout the week.

All hospital pharmacists are urged to attend the Annual Meeting and take an active part in the affairs of the SOCIETY. Since the SOCIETY was organized in 1942 the membership has grown to more than 2,300.

Statue of Liberty

A.Ph.A. Sessions

Hospital pharmacists will also participate in the A.Ph.A. meetings, which will be held throughout the week of April 28. This will be the one hundred and fourth meeting of the A.Ph.A. and it is significant in that it is held in New York City where the first call for a meeting of pharmacists to form a national organization was held in 1851. Other national conventions of the American Pharmaceutical Association were held in New York City in 1855, 1860, 1867, 1907, 1919, and 1937.

The General Sessions, the meetings of the A. Ph.A. House of Delegates, and the various sections will meet on Wednesday, Thursday and Friday. The section meetings to be held during the week include: The Scientific Section, the Section on Education and Legislation, the Section on Pharmaceutical Economics, and the Section on Historical Pharmacy. Further details regarding the program will appear in the March issue of the *Practical Pharmacy Edition of the Journal of the American Pharmaceutical Association.*

Hotel reservations may be made through the Convention Housing Bureau and all members will receive a form listing complete information as to cost and hotel location.

PICTURES BY N.Y. CONVENTION AND TOURIST BUREAU

Times Square

Program

The SOCIETY's Committee on Program and Public Relations, headed by Grover C. Bowles, Chief Pharmacist at Baptist Memorial Hospital in Memphis, Tenn., is in charge of the Program. The following papers have been scheduled for presentation during the general sessions on Monday and Tuesday:

"Some Aspects of the Product Duplication Problem in Hospitals," by August Groeschel, Associate Director, Society of New York Hospital, New York, N. Y.

"Council Evaluation of Recent Drugs," by H. D. Kautz, Secretary, Council on Pharmacy and Chemistry, American Medical Association, Chicago, Ill.

"The Role of the Hospital Pharmacist in the Control of Poisoning," by Edward Press, Field Director, The American Public Health Association, Inc., New York, N. Y.

"Evaluation of a Pharmaceutical Service in Hospitals," by George F. Archambault, Pharmacist Director, Chief, Pharmacy Branch, Division of Hospitals, Bureau of Medical Services, U. S. Public Health Service, Washington, D. C.

"Control of Duplication in the Absence of a Formulary," by James W. Mitchener, Chief Pharmacist, and Rudolph W. Hardy, Assistant Chief Pharmacist, Cabarrus Memorial Hospital, Concord, N. C.

"A Method of Handling Drug Samples," by Louis P. Jeffrey, Chief Pharmacist, Albany Hospital, Albany, N. Y.

"Some Errors in Dispensing Medication and How to Minimize or Avoid Them," by Robert C. Bogash, Director of Pharmacy Service, Lenox Hill Hospital, New York, N. Y.

"Applying Work Simplification to Hospital Pharmacy," by Norman Baker, Apothecary-in-Chief, The New York Hospital, N. Y.

"A Preliminary Laboratory and Clinical Investigation of Novobiocin Sodium in Ophthalmology," by Margaret F. Sherwood, Ronald M. Wood, and W. Arthur Purdum, Chief Pharmacist, The Johns Hopkins Hospital, Baltimore, Md.

"Preparation and Use of Procedural Manuals," by M. R. Kneifl, Executive Secretary, Catholic Hospital Association, St. Louis, Mo.

"Qualifications and Responsibilities of Lay Help in Hospital Pharmacy," by George F. Archambault, Pharmacist Director, Chief, Pharmacy Branch, Division of Hospitals, Bureau of Medical Services, U. S. Public Health Service, Washington, D. C.

"A Pharmacy Salary Plan and Its Significance to the Hospital," by Robert L. Lantos, Chief Pharmacist, University of Texas-Medical Branch, Galveston, Tex.

"Objectives of Education and Training for Hospital Pharmacy Practice," by Don E. Francke, Chief Pharmacist, University Hospital, Ann Arbor, Mich.

"The Utilization of Plastics in the Hospital Pharmacy," by John W. Webb, Pharmacist, Massachusetts General Hospital, Boston, Mass.

"The Current Status of Disposable Needles and Syringes," by Milton W. Skolaut, Chief, Pharmacy Department, Clinical center, National Institutes of Health, Bethesda, Md.

"Hospital Pharmacy Internships—A Historical Record," by Alex Berman, Assistant Professor of Pharmacy, University of Michigan, Ann Arbor, Michigan.

"The Practice of Pharmacy in West Germany," by Glenn Sonnedecker, Secretary, American Institute of the History of Pharmacy, University of Wisconsin, Madison, Wis.

"Pharmacy in the Indian Health Service," by Allen J. Brands, Indian Service, U. S. Public Health Service, Dept. of Health, Education, and Welfare, Washington, D. C.

"Must This Injection Hurt," (Abstract) by Randall Tinker, Assistant Professor of Research, University of Florida, School of Pharmacy, Gainesville, Fla.

In addition to the papers scheduled, a highlight of the Meeting will be a Debate on the following resolution with representatives of the American Association of Colleges of Pharmacy and the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS participating:

"Resolved, that training in hospital pharmacy, not complemented with or accompanied by further academic training, is not in the best interest of the future developments of hospital pharmacy and the profession."

Debaters representing the AACP will take the affirmative side while representatives of the SOCIETY would present the negative side.

This part of the program is scheduled at 11 A.M. on Tuesday, April 30 as a Joint Meeting of the American Association of Colleges of Pharmacy and the ASHP.

Empire State Building

selected pharmaceutical abstracts

and summaries of other articles interesting to hospital pharmacists

edited by LEO F. GODLEY

INTRAVENOUS FAT EMULSIONS

The Preparation and Use of Anhydrous Fat Emulsions for Intravenous Feeding and Metabolic Experiments. D. B. Zilversmit, N. K. Salky, M. L. Trumbull and E. L. McCandless, J. Lab. & Clin. Med. 48:386 (Sept.) 1956.

A stable fat emulsion concentrate is prepared using 10 grams of alcohol-soluble soybean phosphatide suspended in 100 ml. of glycerin by vigorous agitation with a Waring Blendor. When the phosphatide is dissolved, 100 ml. of coconut oil is added and stirring continued for 2-3 minutes. The mixture is essentially an anhydrous base which prevents the hydrolysis of the glycerides normally occurring in an aqueous media. Finely dispersed emulsions of 10-20% fat content suitable for intravenous injection can be prepared by diluting the base with an appropriate amount of water or 5% glucose and shaking manually.

In these animal experiments conducted on dogs, little attention was paid at first to the sterility of the fat emulsion. In later experiments all ingredients except the phosphatide were autoclaved before mixing in the sterile Waring Blendor. Concentration of glycerin above 4 ml. per kilogram of weight gave rise to convulsions. This could be controlled by sedation with Nembutal.

A. J. GIBSON

PYROGENS

The Action of Ion Exchange Resins on Pyrogens, Part I; Effect on the Pyrogenicity of Tap Water, Whittet, T. D., J. Pharm. & Pharmacol. 8:1034 (Dec.) 1956.

Experiments were carried out to determine whether demineralized water is apyrogenic and if so, to ascertain which ion exchange resin is responsible for removal of the pyrogen.

The resins used were Zeocarb 225 (cation exchanger) and Deacidite FF (anion exchanger) in proportions necessary for demineralization. The source of pyrogen was London tap water.

Results obtained from the injection of rabbits with untreated tap water, uncharged Zeocarb treated water, uncharged Deacidite treated water, and Zeocarb-Deacidite treated water are recorded in tabular form. The data indicates that it is possible to produce large quantities of pyrogen-free deionized water from London tap water by passing it successively through columns of the charged cation and anion exchange resins. The uncharged resins have practically no effect on the pyrogenicity.

Further experiments were performed to ascertain which of the resins is responsible for the removal of pyrogens. Pyrogenic tap water was passed through the Zeocarb column and Deacidite column separately. Results of the effect of individual charged ion exchange resins on pyrogenic tap water are recorded in tabular form. The data indicates that charged cation exchange resins have practically no effect on the pyrogenicity; whereas the anion exchange resin is responsible for removing the pyrogenicity from the water.

CLIFTON J. LATIOLAIS

INACTIVATION OF PRESERVATIVES

The Interference of Nonionic Emulsifiers with Preservatives II. de Navarre, M. G. and Bailey, H. E., J. Soc. Cosmetics Chemists 7:427 (Sept.) 1956.

The author's survey of the literature disclosed reports of the interaction of nonionic emulsifiers, such as Tweens, Spans and Carbowaxes, with preservatives, antiseptics and antibiotics. Spans and Tweens were tested against 7 bacteria commonly associated with product spoilage and Sabourand dextrose agar at *p*H 5.6 using benzoic and scorbic acids and methyl *p*-hydroxybenzoate. Benzoic and sorbic acids in concentrations up to 0.2% were ineffective preservatives with Tweens, while methyl *p*-hydroxybenzoate was more effective. Mixtures of some Spans and Tweens resulted in less inactivation of the preservatives.

Complex formation between the polyethylene glycol derivatives and the preservatives is likely, although evidence is inconclusive as indicated by infrared transmission data.

NORMAN HO

MANAGEMENT OF OFFENSIVE ODORS

Effective Management of Offensive Odors, Golden, T., and Burke, J. F., Gastroenterol. 31:260 (Sept.) 1956.

A clinical study was done to evaluate the effectiveness of chlorophyll on offensive odors from infected wounds, ulcerations, colostomy, ileostomy and fecal fistulas.

Experimental chlorphyll preparations used for the study contained 50 mg. water soluble chlorophyll derivatives (100% concentration, NNR) in oil suspension, bulk supplies of the liquid used in the gelatin capsule and tablets containing 100 mg. of water soluble chlorophyll derivatives (100% concentration, NNR). These tablets provided 6-8 times the amount of chlorophyll found in commercial preparations.

In the 50 patient study, it was found that the 100 mg. tablet was the most convenient and effective form. Dosage varied in individual cases from one tablet a day to two tablets four times a day. Success in deodorizing these difficult cases was directly attributed to the high potency of the preparation used. In spite of the high dosage ingested by some patients, no undesirable side effects were observed.

CLIFTON J. LATIOLAIS

DETECTION OF BARBITURATES

Detection and Identification of Clinically Important Barbiturates. Levi, L. and Hubley, C. E., Analyt. Chem. 28:1591 (Oct.) 1956.

Clinically important barbiturates in commercial preparations can be made to react with aqueous copper sulfate-pyridine solutions to give characteristic dark purple-colored $(barbital)_2\ Cu(pyridine)_2$ complexes. Maximum sensitivity of the reactions is attained when the pyridine-water and the pyridine-copper sulfate ratios are minimal indicating the dependence of the reaction on *p*H. The mechanism of action is illustrated. The infrared absorption spectrum of both the barbituric acids and their copper-sulfate-pyridine complexes is given and interpreted. The distinguishing and specific characteristics of the spectrum for the compounds make this method a valuable tool for micro-chemical identification and detection of barbiturates.

NORMAN HO

PURIFIED WATER

Water for Pharmaceutical Purposes, Saunders, L., and Shotton, E., J. Pharm. & Pharmacol. 8:832 (Nov.) 1956.

Without further purification, potable water is not suitable for many pharmaceutical and chemical purposes. Impurities in potable water which necessitate its further purification for pharmaceutical purposes are: (1) micro-organisms and their breakdown products and (2) inorganic salts and dissolved gases. Potable water, sanctioned in the B.P.C. 1954 and NF X for making oral and other preparations, does contain dissolved salts, such as calcium, which affects the sol viscosities and gel strengths of pectin and alginate dispersions.

Two methods of purifying water are (1) distillation and (2) removal of impurities by means of solid reagents (ion exchange resins).

Distillation involves high power and maintenance costs. To reduce these costs, two new methods for electrical heating of water in continuous stills have been developed. One of these is the use of a bare nichrome element immersed in the water. The second heating method uses carbon electrolytes which are immersed in the water to be distilled.

Development of stable ion exchange resins containing strongly ionized acidic and basic groups has led to an important new method for purifying potable water, which is recognized by both USP XV and B.P. addendum, 1955 for preparing water suitable for pharmaceutical purposes other than for injection.

Resins now used for purifying water consist of hard insoluble beads of a styrene-divinylbenzene polymer. The cation exchanger has sulfonic acid groups while the anion exchanger contains quaternary ammonium hydroxide groups distributed throughout the mass. Rate of decomposition of resins is slow; they have a long life and can be regenerated hundreds of times. As a result, ion-exchange process is much cheaper than distillation for purifying water.

The ion-exchange treatment of potable water is more effective than distillation in removing ionized substances from potable water. But demineralized water may contain other contaminants. Albuminous substances and other non-ionic matter may be present in deionized water. Deionized water may be heavily contaminated with micro-organisms unless the de-mineralizing plant is operated under properly controlled conditions with frequent regeneration and back-washing of the column.

Demineralized water can be used in place of distilled water for oral and external use and for preparing stock solutions of chemical reagents, as well as for use as a final rinse liquid in washing glassware.

Problems encountered with the storage of distilled water apply equally to demineralized water. In storage two types of contamination occur (1) growth of micro-organisms and (2) chemical impurities due to the solvent properties of water on container and closure materials during prolonged storage. Sterilization eliminates bacterial contamination; whereas polyethylene containers prevent chemical contamination.

CLIFTON J. LATIOLAIS

HOSPITAL SOLUTIONS

A Comparison of Parenteral Solutions Made by Hospitals and by Industrial Concerns, Glen J. Sperandio, Bull. Parenteral Drug Assoc. 10:4 (Sept.-Oct.) 1956.

A study was made to compare parenteral solutions manufactured by different sources and to actually measure in a quantitative sense some of their properties. A one liter sample each of isotonic sodium chloride solution and dextrose 5 percent in water were obtained from 26 different hospitals who prepared their own and from five established commercial manufacturers to test these solutions for their labeled strength, sterility, and pyrogen content.

Each sample of solution received was coded so the analyst did not know the source. The solutions were subjected to three tests (1) sterility test, (2) pyrogen test, and (3) assay for chemical strength.

The analyses of the hospital made solutions showed the following results. All the solutions were considered sterile. In the pyrogen tests all solutions except one were pyrogen-free. The chemical assay indicated that of the 26 hospital made sodium chloride solutions, nine did not meet the U. S. P. requirements. The majority of the solutions were within 10% of the labeled strength but two solutions varied as much as 20%. Fifty percent of the hospital made dextrose solutions failed to meet the official requirement for labeled strength. For the labeled 5% solutions of dextrose tests showed that the actual concentrations ranged from 3.79% to 10.86%. Seventy one percent of the unsatisfactory solutions were over the maximum strength allowance.

All solutions obtained from the commercial manufacturers were found to be sterile, free of pyrogens, and within limits on chemical strength.

The frequency with which hospitals test their own solutions for sterility, pyrogen content and potency is indicated in table form.

CLIFTON J. LATIOLAIS

STABILITY OF B VITAMINS

Stability of B Vitamins in Pharmaceutical Products. Wokes, F. and Norris, F. W., Pharm. J. 177:263 (Sept. 29) 1956.

Maximum stability of multivitamin products is best achieved when stored in airtight containers in a cool, dry, dark place. Overages of 10 to 20% should be sufficient to insure the potency of the vitamins during normal shelf life. Riboflavin is less stable in liquid than in dry preparations.

NORMAN HO

ABSORPTION OF GERMICIDES BY RUBBER

An Examination of Rubber Used As A Closure for Containers of Injectible Solutions, W. T. Wing, Part I. Factors Affecting the Absorption of Phenol, J. Pharm. and Pharmacol. 7:648 (Oct.) 1955; Part II. The Absorption of Chlorocresol, J. Pharm. and Pharmacol. 8:734 (Oct.) 1956; and Part III. The Effect of the Chemical Composition of the Rubber Mix on Phenol and Chlorocresol Absorption, J. Pharm. and Pharmacol. 8:738 (Oct.) 1956.

Different rubber compositions, time, temperature and concentrations of phenol solutions affected the rate and extent of phenol absorption by rubber. The determination was done in a Spekker absorptimeter using Folin-Ciocalteau reagent in an alkaline medium. The particular composition of rubber samples was outlined. Samples of one type were sealed in tubes with different phenol concentrations and stored at 2° C. and 37° C. The phenol determination was done at various time intervals. Phenol absorption proceeded to the state of equilibrium, the process being determined as reversible. The amount absorbed was directly related to the phenol concentration. The absorption rate increased with the rise in temperature to the point

of equilibrium. The investigation was extended to other type of rubber. The absorption process followed the same general pattern, but the amount absorbed varied with each type of rubber. The alkalinity of various rubber compositions bore inconsistent relationships to phenol absorption. The possibility of phenolic substances in rubber influencing phenol absorption was indicated. The partition coefficient for rubber, decreasing with a rise in temperature and phenol concentration, was established and recommended as a standard for the selection of rubber for pharmaceutical purposes. At the end of the report inquiries were made by several persons on the nature of phenol absorption by rubber.

The method of investigating chlorocresol absorption was the same as for phenol. The results followed the same absorption pattern, but the amount absorbed was less at higher temperatures and higher than phenol.

Phenol and chlorocresol absorption was largely unaffected by the chemical compositions of rubber. The experimental approach was discussed. Increased VN3 (a precipitated silica) and sulfur contents and factice (an oxidation product of linseed oil) increased absorption. Increased zinc oxide concentrations decreased absorption. Santocure affected a lower absorption than the other accelerators. The degree of absorption was influenced by the type of crude rubber used.

NORMAN HO

JOB EVALUATION PROGRAM

How to Develop a Job Evaluation Program, Killingsworth, C. G., Office Executive 31:14 (Dec.) 1956.

A well developed job evaluation program will help to prevent low employee morale, reduced production, increased unit costs, absenteeism and increased labor turnover. A job evaluation program depends upon accurate job descriptions, selection of a basic plan, continuation of the plan, and the attitude of management.

Preparing job descriptions should be done by the employee and checked by the supervisor for accuracy and completeness. Suggestions that will help prepare job descriptions are: (1) prepare a list of duties in inventory style eliminating details; (2) write a logical series of descriptive paragraphs covering each one of the duties listed; (3) avoid using indefinite expressions such as "I handle," etc.; (4) indicate the degree of responsibility. How much accuracy is involved? What checks are required?; (5) indicate percentage of time spent in performing each duty; (6) indicate which duty is felt to be the most difficult and the reason why it is so; (7) indicate which duty requires the most responsibility and the reason why it is so; (8) is there any supervisory responsibility involved? If so, indicate how many people are supervised and give their job titles. Over what functions is direct control maintained? How many decisions will be made that will not require higher approval and to whom is the employee responsible; (9) list any unpleasant features of the particular duty.

There are four basic plans of job evaluation. They are (1) point system; (2) factor comparison; (3) job classification; and (4) ranking method. Each has certain advantages but the point system seems to have more merit.

In the point system one selects certain characteristics that are common to all jobs in your operation. Consider each characteristic as but one aspect of the job as measured against all other jobs having similar characteristics. To accomplish this, divide each characteristic selected into numerical graduations. Thus each characteristic becomes an individual measuring stick.

The job evaluation program should be a continual process. Re-evaluate jobs that change, old jobs that are combined with others, newly created jobs. Continuity is the key to a successful program.

CLIFTON J. LATIOLAIS

CREATIVE THINKING

Practical Techniques in Creative Thinking, Anon. Management Review 45:207 (March) 1956.

Creative training programs are becoming more numerous among leading corporations. New techniques about creativity now make the study of creative thinking more acceptable to the progressive individual.

How ideas are formed is difficult to determine. But attempts are being made to isolate characteristics associated with creative ability. Professor J. P. Guilford of the University of Southern California lists four factors related to creative ability: (1) problem sensitivity—the ability to recognize a problem; (2) idea fluency - the ability to pile up a large number of alternative solutions to the problem; (3) originality; and (4) flexibility - a person's willingness to consider a wide variety of approaches.

Individuals can become more creative through training. Companies are using two programs to obtain more creative thinking from their employees. The first is education—teaching people to use their innate ability. This can be done by (1) creating an awareness of the importance of new ideas, (2) making a person aware of his creative ability, of factors that favor creative output and of those that block it and (3) developing the favorable factors through a series of exercises requiring the use of imagination in problem solving.

The second or operational type of program relies on conference methods to aid idea production. One technique consists of taking an object or problem, listing all its attributes and then changing them one by one in every conceivable way. As a result some of these ideas may have interesting possibilities.

Another operational technique is brainstorming. A brainstorming session is a conference in which all evaluation and criticism is suspended. Any idea on the problem is welcomed. After all ideas are presented they are evaluated. By such permissive ground rules, a climate is established in which people are willing to express themselves freely. Only a small percentage of these ideas are fruitful but the method is a worthy one.

Another conference method is the Gordon technique. This method seeks only one answer to a problem. Only the group leader knows the problem and the participants discuss the general subject in all its aspects. Relying on full association they follow any avenue their discussion takes within the province of the group leader's desires. The group leader attempts to apply the discussion to the problem and when he sees a suitable solution, he reveals the problem and the group continues to work on it by more conventional methods.

What can you expect from a creative thinking program? In addition to usable ideas, creative training dramatizes to employees the importance of ideas. It also helps to break down barriers to communication between echelons in an organization. Creative thinking helps to improve employee attitudes through the development of confidence in their own ability to produce new ideas.

CLIFTON J. LATIOLAIS

therapeutic TRENDS

edited by WILLIAM JOHNSON

267C—An Antispasmodic

Compound 267C is 1-(1-piperidyl)-6-methyl-3-phenyl-3-heptanol hydrochloride and is closely related in structure to trihexyphenidyl and cycrimine hydrochloride. It has been under study for its influence on parkinsonism. Pharmacologic studies indicate that its principal action is antispasmodic. Toxicity studies in animals and in human beings have revealed no significant unfavorable effects from doses several times the average therapeutic dose. In *Amer. Geriatric Soc. J. 4*:793 (August) 1956, Gianvito *et al* describe the investigation of this drug. The usual difficulties in evaluating the results of therapy are encountered and it is necessary to rely on results of frequent observations and reports from nurses and relatives to make a reasonably reliable evaluation of significant changes. Nine women and 21 men with Parkinson's disease were given 267C. Marked improvement was noted in 8 patients, slight improvement in 15, and no improvement in 7. Side effects were observed in 8 patients. When the effects of 267C were compared with the effects of previous medications, it was found that 267C was better in some cases than atropine, belladonna, or hyoscine, but often less useful than any of these drugs and rarely as helpful as trihexyphenidyl. Compound 267C was supplied by Lederle Laboratories.

Etopalin—A Neurolytic Agent

Etopalin is an 8 percent solution of a specially prepared cellulose in 95 percent ethyl alcohol, adapted for intracranial administration. The method of preparing the solution involves the addition of ethyl cellulose to ethyl alcohol, accompanied by thorough mixing to insure complete solution and proper viscosity. Sterilization is accomplished by standard U.S.P. techniques. Cooper reports the use of this new material in *Am. Geriat. Soc. J. 4*:1033 (Oct.) 1956 in the form of an addendum to a previous article in the same Journal (November, 1955).

Intracerebral injections of Etopalin have been carried out in a series of 100 animal experiments which demonstrated that when this substance is slowly injected a uniform, circumscribed, oval shaped, neurolytic lesion is produced. It is unattended by cerebral edema or other undesirable pathologic effects. Etopalin has also been used in a consecutive series of 100 cases of chemopallidectomy in patients with parkinsonism. It has also been used for the production of small, focal lesions in the frontal lobes in certain cases of selective lobotomy. Etopalin was developed by Ciba Pharmaceutical Products, Inc.

Fluoromar—An Anesthetic Agent

Fluoromar (trifluoroethylvinyl ether) is a clear, colorless liquid with an almost sweet and not unpleasant odor. The faint purple fluorescence on exposure to daylight is produced by a stabilizing agent, 0.1 percent phenyl alpha naphthylamine. Fluoromar is stored in dark brown bottles but it appears to be stable during protracted storage even if exposed to sunlight. The vapor does not react with hot sodalime, and it has been impossible to demonstrate breakdown of the molecule in experiments on animals. Nor is there any evidence that such a breakdown occurs in man. Trifluorination of the ethyl radical of the ether significantly raises the lower limit of inflammability, thereby making the compound less inflammable and very difficult or impossible to ignite in concentrations within the anesthetic range.

Dornette reports in *Calif. Med. 85*:311 (Nov.) 1956 after observation of 80 cases in which Fluoromar was used for inhalation anesthesia that induction was rapid; maintenance although labile, was usually smooth; and recovery of reflexes was rapid. Anesthetic complications were minimal, and postanesthetic complications were limited to nausea and vomiting in no greater incidence than that expected to follow the use of most inhalation anesthetic agents. Relaxation, even in deeper planes of Fluoromar anesthesia, is only partial. The extremities are usually well relaxed and reductions of fractures and dislocations may be accomplished with ease. Relaxation of the mandible for laryngoscopic procedures is difficult to attain, and muscle relaxants given intravenously are pref-

erable in such cases. Fluoromar was provided for this study by the Ohio Chemical and Surgical Equipment Co.

Nalline—As A Diagnostic Aid

A simple test using Nalline (N-allylnormorphine) is described by Terry and Braumoeller in *Calif. Med. 85*:299 (Nov.) 1956 to determine whether a patient is addicted to a narcotic, is an occasional user, or is a nonuser. The actual test consists of preliminary measurement of the diameters of the pupils of the eye with a "pupillometer." Nalline is then administered subcutaneously in a dose of 3 mg. and 30 minutes later the diameters of the pupils are again measured. If the person tested has not been using opiates the diameter of the pupils is reduced by 0.5 to as much as 2 mm. In a person who has been using opiates occasionally but who is not addicted, the pupils will remain unchanged in size. In a person who is addicted, the diameter of the pupils will increase by from 0.5 to 2 mm., the amount of increase in size depending on the degree of addiction. Associated with this pupillary dilation is the development of withdrawal symptoms—gooseflesh, yawning, nausea, and vomiting. As soon as withdrawal symptoms appear, Dilaudid or morphine sulfate should be administered. The observation of gross withdrawal symptoms should not be depended upon for a diagnosis but should be avoided if possible. To some degree patients themselves can control withdrawal symptoms. The pupillary response alone is an accurate, sufficient, and sensitive index of narcotic addiction or of occasional use, or the absence of narcotics. Nalline has little if any effect in the patient who has been using either codeine or meperidine.

Peganone—An Anticonvulsant

Peganone (AC 695) is 3-ethyl-5-phenyl-hydantoin and was derived from a previously studied anticonvulsant (Nuvarone) by substituting a 3-ethyl group for a 3-methyl group. This change was made on the basis of a theory developed by Richards according to which the substitution of an ethyl for a methyl group on the nitrogen in the hydantoin or oxazolidinedione molecule would result in a somewhat less potent but also less toxic drug.

This drug was administered to 108 patients who suffered from epileptic seizures of various types. In *J. Pediat. 49*:728 (Dec.) 1956, Livingston concludes that by comparative tests Peganone may not possess as great anticonvulsant properties as diphenylhydantoin sodium, yet the freedom from side effects together with definite effectiveness in major epilepsy (and, to a lesser extent, psychomotor) should make Peganone quite a worthwhile anticonvulsant. In this series of patients, routine blood counts and urine analyses were made monthly and no abnormalities were encountered. Ataxia, diplopia, and hyperplasia of gums which are commonly encountered with diphenylhydantoin sodium therapy were not observed in any of these patients. A generalized morbilliform skin rash was the only significant side reaction observed. This cutaneous reaction occurred about 10 days after instituting therapy and disappeared 7 or 8 hours after withdrawal of the drug. Further study in a larger group of patients over a more extended period of time will be necessary to properly evaluate this drug. Peganone is being investigated by Abbott Laboratories.

Arginine—Its Effect On Blood Ammonia

The ability of intravenously administered L-arginine hydrochloride to decrease the blood ammonia was investigated in fifteen patients with elevation in blood ammonia and varying degrees of encephalopathy associated with several disease entities. In every case there was a reduction in the ammonia levels of the blood following arginine therapy. Improvement in the mental status of the patient accompanied the fall in blood ammonia. Two of three patients with severe viral hepatitis who were given arginine while in deep coma responded in 24 to 36 hours with marked clinical and biochemical improvement and eventual recovery. The decrease in the level of ammonia in the blood that occurred after administration of arginine was always accompanied by a significant rise in the blood urea nitrogen, suggesting that the effect of arginine on the blood ammonia may be mediated through its role in the urea cycle. Further clinical experience with substances such as arginine which can effectively lower the blood ammonia should serve to delineate more clearly the pathologic importance of ammonia intoxication in clinical disease. Solutions of arginine for intravenous administration were prepared by adding 25 Gm. of L-arginine hydrochloride to 400 ml. of pyrogen-free distilled water, followed by autoclaving at 15 pounds pressure for 20 minutes. Immediately before injection, 100 ml. of 50 percent dextrose were added aseptically, resulting in 500 ml. of a 5 percent solution of arginine hydrochloride in 10 percent dextrose, with a *p*H of 5.9 to 6.1. This work was reported by Najarian and Harper in *Am. J. Med. 21*:832 (Dec.) 1956.

timely drugs

Albamycin Syrup

. . . a stable, rose pink colored, cherry custard flavored, aqueous suspension of novobiocin calcium, has been announced by The Upjohn Co. Albamycin is active against both gram-positive and gram-negative bacteria, and is particularly effective against *S. aureus.* The indications and dosage for Albamycin syrup are the same as for the oral capsules. For adults, the usual dosage is 500 mg. every 12 hours, continued for at least 48 hours after all evidence of infection has disappeared. For children, the dosage is 15 mg. per kilogram of body weight per day, administered on a similar schedule. Albamycin syrup contains 125 mg. of novobiocin calcium in each 5 ml., and is packaged in two ounce and pint bottles.

Butiserpine R-A

. . . recently introduced by McNeil Laboratories, Inc., is a repeat action tablet containing Butisol sodium and reserpine. Each tablet provides the equivalent of two regular doses taken about four hours apart. It is indicated in the treatment of mild to moderate essential hypertension, and as a mild sedative-tranquilizer in such conditions as coronary occlusion, angina pectoris congestive heart failure, anxiety neuroses, and insomnia. Administration of one Butiserpine R-A tablet in the morning provides the patient with a prolonged sedative and antihypertensive action during the working day. Butiserpine Repeat Action tablets are supplied in bottles of 50 tablets.

Compazine

. . . a true tranquilizer and potent antiemetic with minimal side effects, has been announced by Smith, Kline & French Laboratories. It is indicated in mild and moderate mental and emotional disturbances, whether occurring along or in association with somatic conditions, and in mild and severe nausea and vomiting of widely varying etiologies, particularly that of pregnancy. Dosage varies with the individual. In most patients doses of 5 mg. administered three or four times daily, are effective. Some patients require 10 mg. three or four times daily, but only in the rarest instances should the latter dosage be exceeded. Children over 12 should use the lower adult dosage. As yet no dosage has been established for children under 12 years of age. At present Compazine is recommended for relatively short-term therapy (not longer than two weeks).

Since Compazine (proclorperazine, S.K.F.) is a phenothiazine derivative, patients receiving it should be checked regularly for any sign of blood dyscrasia or other toxic manifestations. It is contraindicated in comatose or greatly depressed states due to central nervous system depressants. The potentiating action of Compazine is not as great as that of Thorazine. However, if depressant agents are used in conjunction with this drug, their amount should be reduced by one-half.

Compazine tablets, each containing 5 mg. of proclorperazine as the dimaleate, is packaged in bottles of 50 and 500.

Ecotrin

. . . Smith, Kline & French Laboratories' new Duentric-coated aspirin tablet, makes possible high, long-term dosage of aspirin without gastric upset. It is indicated wherever high doses of aspirin are needed or wherever gastric discomfort makes therapy with ordinary aspirin tablets impractical, particularly in rheumatic disease. Ecotrin, in addition to causing no gastric irritation, is promptly absorbed in the small intestine, and gives full analgesic, antipyretic, and anti-inflammatory effects of aspirin. Suggested dosages are up to 2 Gm. daily in acute rheumatic fever and up to 1.6 Gm. in arthritic conditions. Each Ecotrin tablet contains 0.3 Gm. of aspirin and is packaged in bottles of 100 tablets.

Ilotycin Dental Cones

. . . are now available from Eli Lilly and Company. Dental Cones Ilotycin (erythromycin, Lilly) glucoheptonate are used for the prevention of infection which may follow tooth extractions. An outstanding feature of these is that the cones disintegrate completely in the very small volumes of plasma or serum normally found in an extraction wound. The disintegration and solubility times are between 20 and 40 minutes.

Ilotycin dental cones are primarily indicated for the prevention of the local multiplication of pathogenic or saprophytic bacteria associated with tooth extraction. There have been no reports of post-operative hemorrhage resulting from their use. No contraindications to them have yet been discoverd. As with other topical medication, there is always the possibility of sensitivity reactions in certain individuals.

Each cone contains 5 mg. of erythromycin glucoheptonate. The filler consists of sodium bicarbonate and sodium chloride. For easy insertion, the cones have been compressed into flattened white ovals with rounded ends. Scoring at the center permits use of a half-cone where indicated.

Magnacort

. . . a new steroid developed especially for topical use, has been developed by Pfizer Laboratories. It is a water-soluble, lipophobic dermacoid (dermatologic corticoid)

which facilitates penetration into inflammatory tissue with greater speed and with better diffusion. This also allows dispersion more slowly into the fatty layers with a consequent longer contact at the affected tissue site, at therapeutic levels. Magnacort (ethamicort, Pfizer) ointment is indicated in atopic dermatitis contact dermatitis, nonspecific anogenital pruritis, and miscellaneous dermatitis conditions such as seborrheic, stasis, etc. Extensive clinical investigations report no evidence of systemic side effects.

Magnacort ointment is applied by carefully rubbing on affected areas two or three times daily. In chronic dermatosis, maintenance therapy may be required after eruption has subsided to avoid relapse. In such cases minimum applications are desirable. Once daily or every other day may prove adequate. The ointment is available in 1/6 oz. and 1/2 oz. tubes, each containing 0.5% Magnacort in a petrolatum base.

Moderil

. . . a new alkaloid of rauwolfia, has been announced by Pfizer Laboratories. It is a pure crystalline alkaloid with hypotensive and tranquilizing properties which acts by central depression of the sympathetic nervous system without peripheral blocking, and does not affect cardiac output. Moderil (rescinnamine, Pfizer) brings relief to patients suffering from labile essential hypertension and tension. Side effects are infrequent. Drowsiness and/or nasal congestion may occur and may spontaneously disappear with continued use of the drug without reduction of dosage. Frequency of defecation or loose stools is an occasional reaction, but since the hypertensive patient is usually constipated this effect may be helpful. Because Moderil may increase gastric secretion, it should be used with caution in patients with a history of peptic ulcer.

In order to obviate the possible discomfort from the increased gastric secretion that Moderil may stimulate, doses should be taken after meals. The recommended initial dose is 0.25 mg. administered twice daily for two weeks. The maximum initial dose should not exceed 0.5 mg. twice daily for one week. For maintenance therapy the dosage should then be adjusted to 0.25 mg. once daily. Moderil tablets are supplied as oval, scored, yellow 0.25 mg. tablets in bottles of 100's and 500's, and as oval, scored, salmon 0.5 mg. tablets in bottle of 100's.

Neo-Magnacort Ointment

. . . is now marketed by Pfizer Laboratories. Neo-Magnacort ointment combines the new water-soluble dermatologic corticoid ethamicort (see description of Magnacort in this section of Timely Drugs) and the antibiotic neomycin for superior control of local infections and secondarily infected dermatoses. The ointment is supplied in 1/6 oz. and 1/2 oz. tubes containing 0.5% Magnacort and 0.5% neomycin sulfate.

Plaquenil

. . . for lupus erythematosus, polymorphic light eruptions, malaria, etc., has recently been released by Winthrop Laboratories. It was first introduced as an antimalarial drug having a high degree of clinical safety and effectiveness. Studies with other antimalarials demonstrated the beneficial effect of these drugs upon the lesions of discoid lupus erythematosus. Subsequently Plaquenil sulfate (known as Win 1258 in early studies) was also tried clinically in this and related conditions. Extensive studies prove that this new 4-aminoquinoline is not only useful in the management of discoid lupus as well as in polymorphic light eruption, but also has certain advantages over the earlier drugs. Although the exact mechanism of action is unknown, there is a possibility that the drug screens certain ultra violet wave lengths from sunlight, thereby diminishing the deleterious effect of such rays upon the light-sensitive skin. It is effective in controlling (1) lupus erythematosus: chronic discoid, localized edematous or subacute types; (2) polymorphic light eruptions; (3) malaria due to *Plasmodium falciparum* and *P. vivax;* and (4) Giardia lamblia infection. Side effects are uncommon and related mainly to the gastrointestinal tract. Infrequently dermatitis, lassitude, dizziness, headache, and mild anemia have been noted.

In lupus erythematosus and polymorphic light eruptions the average adult dose of Plaquenil (hydroxychloroquine, Winthrop) sulfate is 400 mg. orally once or twice daily for several weeks or months depending upon the patient response. In prolonged maintenance therapy 200 to 400 mg. daily will suffice. In malaria an initial adult dose of 800 mg. is followed by 400 mg. in from 6 to 8 hours and 400 mg. on each of two successive days (total 2 Gm.). In giardiasis 200 mg. administered three times daily is advised. Smaller doses are recommended for children. Plaquenil sulfate is available as tablets of 200 mg. in bottles of 100.

Rolicton

. . . a non-mercurial oral diuretic, has been introduced by G. D. Searle & Co. It effects a diuresis which, with adequate dosage, is comparable to that obtained with mercurial diuretics administered parenterally. Rolicton (aminoisometradine, Searle) acts by inhibiting the resorption of the sodium ion by the renal tubule, and is indicated for edematous states which are characterized by sodium retention, especially the edema of congestive heart failure. No contraindications have been encountered and the drug may be given in the presence of cardiac, hepatic, or renal disease. Disturbances of electrolyte or acid-base balance have not been encountered; gastric irritation may be manifested in some patients although its incidence only approaches placebo levels.

The usual adult dose of Rolicton is one tablet administered four times daily with meals on the first day of therapy and one tablet twice daily with meals thereafter. The drug is available as uncoated, scored, pale green tablets of 400 mg. each, and is supplied in bottles of 100 and 500 tablets.

Seco-Synatan

. . . a new "modulator" for symptomatic control of anxiety, depression, or obesity, has been released by Irwin-Neisler and Company. The new product Synatan (dextroamphetamine tannate) 17.5 mg. with secobarbital 35.0 mg. A single dose in the morning controls the patient's appetite all through the day and creates a sense of optimism and well-being. In addition, it controls the patient's emotions by producing a calming effect which contributes to the feeling of security

and comfort. The usual dose of Seco-Synatan is one or two tabules at 10 A.M. for all day control.

Sigmamycin

. . . a new broad-spectrum antibiotic combination, is now available from Pfizer Laboratories. It contains the new antimicrobial agent oleandomycin (Matromycin, Pfizer) which extends the effectiveness of broad-spectrum therapy by enhanced activity against existing resistant strains and simultaneously helps to control the emergence of new resistant strains. Sigmamycin exerts a synergistic activity *in vitro* against selected microorganisms, including antibiotic-resistant clinical isolates; has marked ability to retard the emergence of antibiotic-resistant variants of *M. pyogenes* var *aureus* strain 5 and *Str. pyogenes* 8668; and has statistically significant synergistic activity *in vivo* against both normal and antibiotic-resistant *M. pyogenes* var. *aureus* and *Str. pyogenes* infections in mice. Each 250 mg. capsule contains 167 mg. of tetracycline and 83 mg. of oleandomycin.

Sigmamycin is indicated in the following conditions: pneumonia (with or without bacteremia) caused by pneumococci, streptococci, staphylococci, or mixed flora; primary atypical pneumonia; infections of the respiratory tract and related structures; genitourinary infections caused by *E. coli, Aerobacter aerogenes,* streptococci, or mixed flora; surgical infections; and miscellaneous other infections.

Sul-Spansion

. . . a sustained action broad-spectrum antibacterial for the treatment of respiratory, urinary tract and other systemic infections, has been released by Smith, Kline & French Laboratories. Available in a suspension form, it provides prompt, prolonged antibacterial activity around the clock with a single oral dose every 12 hours. Incorporated in this suspension is a safe, soluble and efficacious sulfonamide, sulfaethylthiadiazole. This compound is effective against a wide range of gram-positive and gram-negative organisms, even in many cases where broad-spectrum antibiotics have failed.

In adults and children over 75 pounds, the maintenance dose of Sul-Spansion is one tablespoonful (three teaspoonfuls) every 12 hours; the priming dose is double the maintenance dose. For children up to 75 pounds, the maintenance dose is one-half teaspoonful every 12 hours per 15 pounds of body weight. Each 5 ml. of the suspension contains 0.65 Gm. of sulfaethylthiadiazole.

TACE with Androgen

. . . a new research combination of The Wm. S. Merrell Co., combines TACE, a long-acting oral estrogen, with methyltestosterone, for the control of declining estrogen-androgen levels. It is primarily indicated for use in menopause, osteoporosis, and gerontotherapy. In menopause, the dosage is two capsules daily for 60 days, until relief of symptoms, then one capsule daily. For osteoporosis, the dose is one capsule daily; and in gerontotherapy as replacement therapy management of senescence, one or two capsules are administered daily. Each orange capsule contains 6 mg. TACE and 2.5 mg. methyltestosterone, and is supplied in bottles of 100 capsules.

T. H. & M. Cough Syrup

. . . a palatable, maple flavored suspension contain terpin hydrate and Methorate (dextromethorphan) hydrobromide, is available from The Upjohn Co. Unlike codeine and other opium alkaloids, it produces little or no depression of the central nervous system and does not cause constipation. It does not produce analgesia. It appears to have no addicting effects even after the prolonged use of rather high doses. Its toxicity is low and its side effects minimal. T. H. & M. is effective in alleviating cough associated with the common cold, laryngitis, tracheitis, and bronchitis. For adults the dosage is one to two teaspoonfuls, one to four times daily, the total daily dose not exceeding eight teaspoonfuls. Children four to 12 years of age should receive one-half to one teaspoonful, one to four times daily, the total daily dose not exceeding four teaspoonfuls; and children two to four years of age should receive one-fourth to one-half teaspoonful, one to four times daily, the total daily dose not exceeding two teaspoonfuls.

T. H. & M. cough syrup, each 5 ml. containing 10 mg. Methorate hydrobromide and 85 mg. terpin hydrate, is available in pint bottles.

Trexinest

. . . a new product of Hynson, Westcott & Dunning, Inc. for use in the treatment of the disturbing symptoms associated with the menopausal syndrome, combines the effects of naturally occurring equine estrogens and Lutrexin (lututrin, H.W.&D.). Lutrexin is a water-soluble, non-steroid, uterine relaxing hormone. Clinical investigation indicates that Trexinest tablets produce prompt relief of the distressing symptoms associated with the menopausal syndrome. Dosage schedules vary with cases. Excellent results have been obtained by the administration of one tablet once or twice daily until symptoms are relieved. Many clinicians prefer a maintenance dose of one tablet every other day or two tablets weekly for three weeks, followed by a rest period of four or five days. Each blue, sugar-coated Trexinest tablet contains 1.0 mg. estrogenic substance calculated as sodium estrone sulfate and 250 units Lutrexin. The tablets are supplied in bottles of 50.

V-Cillin-Sulfa Pediatric

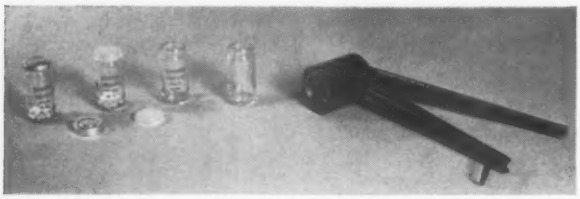
. . . a combination of penicillin V (phenoxymethyl penicillin) and sulfonamides, has been released by Eli Lilly and Company. The medicament is sealed in the dry granules with a water-soluble gum to be released when water is added for dispensing. When reconstituted, the product becomes 60 ml. of a smooth-textured liquid suspension which is bright yellow in color and pineapple-flavored. Each teaspoonful of the suspension contains 125 mg. (200,000 units) of penicillin V, and 167 mg. each of sulfadiazine, sulfamerazine, and sulfamethazine. The usual dose for a 20 pound child is one teaspoonful four times daily (based on sulfonamide content). The combination of oral penicillin and triple sulfas provides a broader spectrum of antibacterial activity, tends to prevent the development of resistant strains, and constitutes a better agent for the control of mixed infections.

Notes and Suggestions

by Milton W. Skolaut

PREPACKAGING NARCOTICS WITH ALUMINUM SEALED CONTAINERS

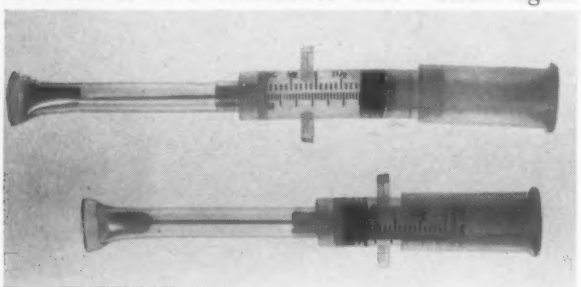
Photograph No. 1 shows the use of round, clear, glass vials with a plastic snap-on lid, which are secured by means of an aluminum seal. It



is a single seal with a tear-off tab, which makes the contents of the bottle tamper-proof, since it cannot be removed and replaced. This replaces the Celons, which are not entirely tamper-proof, and therefore, with the aluminum seals the Pharmacy Department can guarantee the contents and count until the aluminum seal is broken.

DISPOSABLE SYRINGES AND NEEDLES

Accompanying is a photograph of a polyethylene disposable syringe with a molded needle, which will soon be available commercially for distribution at a reasonable cost. These again

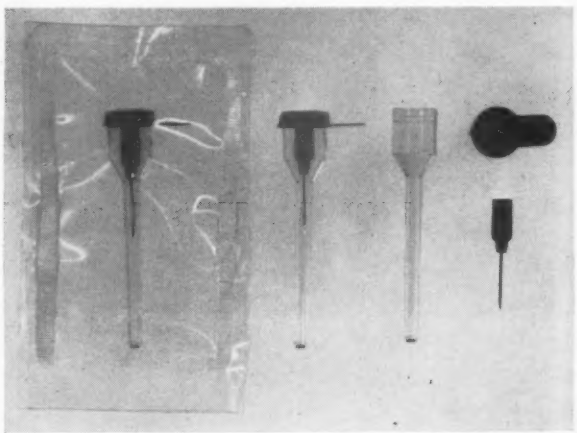


are economical when they are used in quantity in the most popular sizes. The seal between the plunger and barrel is made by a rubber gasket attachment at the end of the plunger which makes it quite satisfactory for use. The feel of the syringe is somewhat lighter than the normal glass ones. Thus, it does require a slight change in technique but it is found satisfactory after the personnel become accustomed to the new feel.

Milton W. Skolaut is Chief, Pharmacy Department, Clinical Center, National Institutes of Health, Bethesda, Maryland.

DISPOSABLE NEEDLES

There have been numerous articles in journals concerning disposable needles. There have been cost figures showing that they are more expensive or less expensive, but now there are available on the market, sterile disposable needles packaged in a safe and lasting container which provides and guarantees sterility for an almost indefinite period. The accompanying photograph shows

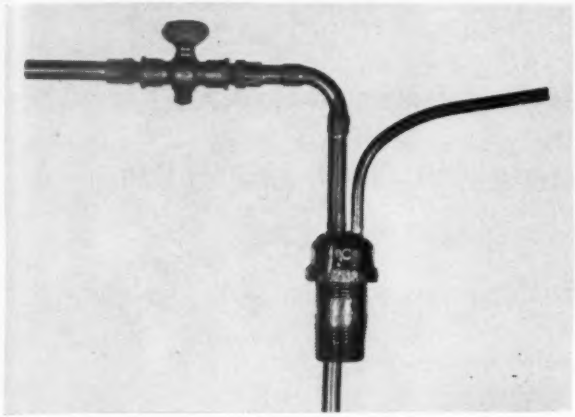


the final packaging adapted for our use, eliminating the processing and dangers connected with the type and size of needles which are most popular. They are available in approximately seven to eight sizes at the present time but are most economical in the very commonly used sizes only. They have been found to be very satisfactory and in some cases do save considerable manpower.

AIR PRESSURE FOR REMOVING ALCOHOL FROM DRUMS

Numerous methods have been devised for draining alcohol from the bulk drums into smaller containers, when it was necessary. The system used at the National Institutes of Health is merely air pressure (10 pounds per square inch) which has been connected to the house air line and is introduced into the drum through a dual pipe attachment through the small bung hole. The short pipe connection allows the introduction of the air under pressure. A long pipe starts at approximately ¼ to ½ inch from the bottom of the tank and is introduced through the bung attach-

ment and is then connected to a hose attachment with the cut-off in the metal pipe, prior to the



hose attachment. This way only the small bung hole has to be opened. The drum may be left sitting in its upright position and the removal of the alcohol is very simple.

DROPPER BOTTLE RINSER

The accompanying photograph shows a small adaptation of an irrigating solution bottle rinser, which was built for use with dropper bottles. A

problem has existed during past years in the rinsing of dropper bottles with distilled water, when it was required or desired. This hastens the work and it also can be used for any narrow neck bottle which is to be rinsed with distilled water. It is permanently connected to the normal distilled water bottle by means of a "T" tube so that the normal draw cock is available at all times.

ECONOMIC POISONS BOOKLET

The U. S. Department of Health, Education, and Welfare has issued a "Clinical Memoranda on Economic Poisons". They have been prepared primarily for the guidance of physicians in the diagnosis and treatment of persons who may have had extensive or intensive exposure to pesticides; however, they contain general information which may be of interest to others also. A part of each memorandum is devoted to a description of the chemical nature, formulations, and uses of the compound under consideration. Copies of this 78-page booklet may be obtained for thirty cents from the Superintendent of Documents, U. S. Government Printing Office, Washington 25, D.C.

SILICONE BOOKLET

Dow Corning Corp., Midland, Mich., has issued its 1957 Reference Guide to Dow Corning Silicones. The booklet describes nearly 150 commercially available silicone products. Brief descriptions are given of the various silicones, and comparative charts are made of the silicones and the materials which they are replacing. Copies of this 12-page brochure may be obtained directly from Dow Corning.

NARCOTIC RECEIPT SHEET

Following is a copy of a new narcotic receipt portion on the narcotic recording sheet, which gives the Pharmacy a tighter control system concerning the disposition narcotic record. The narcotic requisition and disposition sheet (not shown) are very similar to the ones used by the Public Health Service for some years but now a narcotic receipt for the disposition record has been added. This greatly reduces the frequency of loss of the disposition record and the pin-pointing of the blame for such losses. On occasions, records have been lost, and the Nursing Department has claimed that they have been returned to the Pharmacy —and the Pharmacy has no such record. This gives a receipt, if it was returned, and the proper blame can be fixed if lost.

PHS-2621 (PART III)
7-56

RECEIPT FOR COMPLETED CERTIFICATE OF DISPOSITION

DRUG	STRENGTH	QUANTITY	DATE / RECEIPT NO.

FORM (Specify) ☐ TABLET ☐ INJECTION ☐ LIQUID ☐ OTHER	NURSING UNIT	FORM AND CONTAINER RECEIVED BY (PHARMACIST)

PHARMACIST WILL DETACH RECEIPT AFTER SIGNATURE AND ACCEPTANCE OF COMPLETED CERTIFICATE OF DISPOSITION AND EMPTY CONTAINER.

Impressions...

an American pharmacist in Europe

by GLENN SONNEDECKER, *Secretary, American Institute of the History of Pharmacy*

Fourth in a series of informal columns dispatched to THE BULLETIN by Dr. Sonnedecker during his year in Europe as a Fulbright Research Scholar and Fellow of the Guggenheim Foundation.

The German University Student

THE JOHANN WOLFGANG GOETHE University, here in Frankfurt am Main, still struggles to mend the damage to faculty and facilities that began with erosion by National Socialism and ended with destruction by bombs. That can be said of most German universities, although they again have reached a high standard of work.

Pharmacy may be studied at 13 of the 16 West German universities and at three of the eight technical colleges (i.e., "technische Hochschulen" that confer degrees similar to those of a university). Bombs destroyed at least seven of the pharmacy departments, wholly or in part, but all are functioning again and five are in new buildings or soon will be.

The university students look and act more mature, on the average, than American students. All but 12.4 percent of German students are at least 21 years old, according to a study in 1953. And responsible attitudes no doubt are encouraged by the relatively rigorous demands and discipline in the type of secondary school from which university students have graduated. A boy tells me, for example, that half of his class in the "Gymnasium" failed this semester in one or the other subject. Only about 15 percent of German youth can surmount such a hurdle and thus qualify to enter a university. The majority attend various other kinds of secondary school.

When a student receives a Gymnasium diploma he already has a general education equalling perhaps two years of study in most American colleges and universities. But the systems are so different that one dare not push comparisons too far.

A German university offers the "freshman" student a degree of freedom and responsibility that seems remarkable to Americans. The student has a wide choice in the lectures he wishes to hear—although the "suggested" curricula are more confining in professions that require state examinations. In any event, a student ordinarily does not attend lectures for which he has signed up unless he wants to. On the other hand, he may hear a subject not only once, but several times from different professors to compare their points of view. The idea of "taking a course," once and for all, does not hold the central place that it does among American students. The student customarily has not fixed reading assignments and no examinations. There may be an examination, especially in technical fields, for admission to a seminar or higher level of study.

He receives no grades. During his university career it is "only" necessary that the student obtain sufficient knowledge, in some way, for the profession he wishes to profess. And this he must clearly demonstrate in a comprehensive examination at the end, before he receives a state or academic degree.

At most German universities the students do not know the "campus life" of their American counterparts. Usually, there is no campus, the various "institutes" being scattered about a university town. But new construction often suggests an American pattern, particularly the opening of "student union" buildings (sometimes with American aid) and dormitories.

Universities are crowded; indeed, there are more students in West Germany now than there were in the whole of Germany a quarter century ago. Many students (30 to 40 percent) earn at least part of their expenses by working during the school year—many more than in former times. This circumstance, coupled with the progressively larger number of students per teacher, is seriously discussed as a threat to traditional academic standards. Curiously, in the pharmacy departments there are more students per teacher of professorial rank than in any other field of university study. More interesting still, almost half of the pharmacy students are women, while about 16 percent of the student body as a whole consists of women. This probably finds explanation largely in the limitation on the number of pharmacies, which makes the prospect of owning a pharmacy rather discouraging for ambitious young men.

The pharmacy students have had two years of controlled experience in selected pharmacies, and a preliminary examination, before they come to the university. Here they take at least six semesters of study, followed by a state examination and one year of probationary practice before receiving the full qualification.

SPECIAL PROJECTS

ASHP Committee Urges Participation

by BENJAMIN TEPLITSKY, *Chairman*

THE COMMITTEE ON SPECIAL PROJECTS of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS was initiated during the presidency of Walter Frazier in 1951-1952. Numerous accomplishments of importance to the practice of hospital pharmacy have occurred since then. The program on special projects makes it possible for each Affiliated Chapter to participate in the aims of the National Organization.

Under the leadership of such chairmen as Paul Parker, Robert Bogash, Evlyn Gray Scott and Henry Beard, great strides have been made. It is interesting to note that twenty-four Affiliated Chapters have responded thus far this year and are engaged in twenty-eight projects.

A project may be as simple as requesting members of different hospitals to submit outstanding formulations or requesting different pharmacies to submit the ratio of antibiotic prescriptions to all others. Any such pooled statistical information presents a trend or picture otherwise not visible. Naturally, projects may be more elaborate.

It is urged that each Affiliated Chapter appoint a standing or a Special Committee on Special Projects and that such committee be in contact with the national committee in regard to various projects in progress. With the aid of the membership of the Chapter, many interesting facts may be amassed and in turn be converted into practical and worthwhile projects.

The projects reported thus far from the SOCIETY's Affiliated Chapters are:

1. Survey of Poisonings
2. Pharmacy Law
3. Asepsis in Ophthalmic Solutions
4. A History of the Texas Hospital Pharmacy Seminars
5. Accidental Poisonings
6. A Survey of Hospital Pharmacists in Indiana in an Attempt to Raise Classification and Salaries of State Employed Pharmacists
7. A Study of State Mental Hospital Pharmaceutical Services with Proposals for Improvement of These Services
8. The Survey of Hospital Pharmacy in Iowa
9. Program to Arrange for Pharmacy Students to Visit Hospital Pharmacies
10. Seminar on Sterile Solutions

Benjamin Teplitsky

11. Better Public Relations
12. Survey of Salaries for Chief Pharmacists, Staff Pharmacists, and Pharmacy Interns in North and South Carolina
13. Survey of Charges to Inpatients in North and South Carolina.
14. Dissemination of Information Concerning Accidental Poisoning in Children.
15. Insurance Committees
16. Board of Pharmacy—Public Health
17. Common Household and Economic Poisons and Antidotes
18. Hospital Pharmacy's Active Assistance in Civil Defense and Disaster Planning Organization
19. Maintaining of Register of All Hospital Pharmacists in the State of Illinois
20. Civil Defense Program in Dade County (Florida)
21. Increasing Membership in the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS
22. Problems of Medications in Small Hospitals and Nursing Homes
23. Information Files
24. Mechanisms of Getting Information to Nurses, Interns, Residents and Physicians
25. Contracts, Laws and Insurance
26. Improving Administrator-Pharmacist Relationships by Forming a Consultant Committee to Aid Administrators
27. History of Hospital Pharmacy in the Houston Area
28. History of the Houston Area Society of Hospital Pharmacists

It is the desire of the National SOCIETY that each Affiliated Chapter initiate one or more projects and in so doing become actively engaged in promoting the advancement and service of hospital pharmacy as well as its prestige.

Committee on Special Projects: James D. McKinley, Houston, Tex.; Eugene O. Hovis, Massillon, Ohio; Ruth Pully, Torrington, Conn.; Sister Mary Carl Marty, Jackson, Miss.; and Benjamin Teplitsky, *Chairman*, 34 Niblock Court, Albany, N. Y.

PRE-CONVENTION
CONFERENCE
ON PARENTERAL PRODUCTS

conducted by the Philadelphia Hospital Pharmacists' Association

A PRE-CONVENTION CONFERENCE on the preparation of parenteral products by the hospital pharmacist will be conducted by the Philadelphia Hospital Pharmacists' Association at Hotel Statler, New York City, Saturday April 27, 1957, with registration beginning at 9:30 A.M.

The conference will consist of a series of six discussion periods in which an expert will present certain areas of the subject during the first 15 minutes, with the remainder of each hour being spent in a question and answer period with the audience participating. The expert will, according to Herbert L. Flack, President of the Association, "set or begin the 'train of thought' in a direction so that the audience may 'climb aboard' and travel with him to the 'terminal'."

The tentative program of the conference is as follows:

9:30 A.M. Registration in the Georgian Foyer, Statler
10:00 A.M. Relationship of Glass Composition to Stability of Formulations by Joseph P. Majeske, Director of Research, T. C. Wheaton Co., Millville, N. J.
11:00 A.M. Selection of Filters by Dr. Kenneth Avis, Assistant Professor in Pharmacy, Philadelphia College of Pharmacy and Science.
12:00 noon Pressure Steam Sterilization, a color, sound film.
12:30 P.M. Lunch
1:30 P.M. Steam Sterilization by John J. Perkins, Director of Research, American Sterilizer Co., Erie, Pa.
2:30 P.M. Washing of Glassware by Eugene Barclay, Director of the Biological and Sterile Pharmaceutical Laboratories, Merck Sharp & Dohme, Division of Merck & Co., Inc., West Point, Pa.
3:30 P.M. Coffee Break
3:45 P.M. The Hospital Pharmacist's Responsibility in Testing by Dr. Louis Gershenfeld, Professor of Bacteriology and Hygiene and Director of the Department of Bacteriology, Philadelphia College of Pharmacy and Science.
4:45 P.M. Open Panel Discussion on Problems Undiscussed or Insufficiently Discussed in the Previous Sessions. The program speakers plus several hospital pharmacists will comprise this panel.
6:00 P.M. Social Hour; 7:00 P.M. Dinner.

Since there is limited seating capacity available, and since reservations for the lunch and dinner must be made in advance, it is requested that all hospital pharmacists who plan to attend all or a part of this conference make known their intention and register by April 19th by writing to Mr. Herbert Flack, Director of Pharmacy Service, Jefferson Medical College Hospital, Philadelphia 7, Pa.

Special Summer Courses to be Available

The Philadelphia Hospital Pharmacists' Association and the Philadelphia College of Pharmacy and Science are cooperating to offer three special courses during the summer of 1957. From June 17 through June 28, Dr. Grafton D. Chase, Assistant Professor in Chemistry at the College, will conduct lecture and laboratory periods in "Radioisotope Techniques." During the period July 8 through July 19, Dr. Chase will conduct laboratory and classwork in "Analysis of Medicinals."

During the period from June 17 through June 28, and to be repeated from July 8 through July 19, Dr. Kenneth Avis, Assistant Professor in Pharmacy at the College, will conduct laboratory and classwork in the "Preparation of Parenteral Products." These courses are offered primarily for, and teaching is directed toward, pharmacists practicing in hospitals.

The classroom space in each of these groups is limited. Early registration is advisable. The fee for each of these courses is $65.00. Further details may be obtained through the Registrar of the Philadelphia College of Pharmacy and Science, 43rd Street, Kingsessing and Woodland Avenues, Philadelphia 4, Pa., who will assist also in securing rooming accommodations for those who come to Philadelphia from distant cities.

The course in "Analysis of Medicinals" will include, where possible, work on both the official assay and on a "control" assay for each type of preparation or substance normally prepared in bulk by hospital pharmacists, and also will include rapid tests or checks for adulteration or "watering" of narcotic injections, and other valuable data.

ASHP affiliates

Cleveland Society

Officers of the Cleveland Society are as follows: *President* Robert Stockhaus, University Hospitals of Cleveland; *Vice-President* Samual Steinberg, Mt. Sinai Hospital; *Secretary* Klotilda Baclowski, University Hospitals of Cleveland; and *Treasurer* Freda Escavage, Doctor's Hospital.

Among recent activities of the Cleveland Society was a Seminar which was sponsored in cooperation with Pfizer Laboratories early in December. Mr. Leo Godley, President-Elect of the SOCIETY, was among the principal speakers.

Washington State Hospital Pharmacists

Twenty-nine members were present for the September 11 meeting of the Washington State Hospital Pharmacists. President Roberta Dodds presented a tentative schedule for the 1956-1957 meetings and there was general discussion regarding the programs and places as scheduled. Other business covered during the meeting included the Treasurer's report, a motion to make a contribution to the A.Ph.A. Building Fund, consideration of projects to raise money, and plans for a special meeting in October which would coincide with a visit from the President of the National SOCIETY, Mr. Paul Parker.

Following the business session, a movie entitled "Modern Operative Cholangiography," was shown. The meeting was held at the Swedish Hospital in Seattle with pharmacists at the Institution serving as hosts.

Oklahoma Society

The October 18 meeting of the Oklahoma Society of Hospital Pharmacists was held in the Medical Library of the St. Anthony Hospital in Oklahoma City. Sister M. Teresa, President, called the meeting to order and after a brief welcome introduced the speaker of the evening, Dr. Ralph Bienfang, Professor of Pharmacognosy from the College of Pharmacy, Norman, Oklahoma. Dr. Bienfang presented to the group his second fancied "time trip" to visit Pharmacist Gnafneib in the year of 1976. His paper was entitled "Pharmacist Gnafneib Revisited—A Fantasy." His paper gave the group an idea of what pharmacists could do in the future to better their position as professional people.

During the business session plans were made for the Annual Convention of the Oklahoma Society of Hospital Pharmacists which was scheduled in Oklahoma City for November 8. At that time, Mr. Paul Parker, President of the ASHP, was one of the principal speakers.

Arizona Society

Mr. Paul Parker, President of the ASHP, was the guest speaker for the October 21 meeting of the Arizona Society of Hospital Pharmacists. In his discussion he pointed out that health is rapidly growing in importance to the people of the world and, as it does, there are more and more specialized needs which hospital pharmacists must learn to meet.

The meeting was held in the Sky Room of the Sahara Motel in Phoenix.

Society of Greater Kansas City

The Society of Hospital Pharmacists of Greater Kansas City met at the Kansas City University College of Pharmacy on October 16 at 2 P.M. with fourteen members present. Much of the time was devoted to continuing a discussion on cooperating with the School of Pharmacy in presenting a course in Hospital Pharmacy which is to be scheduled in the spring. Also, there was some discussion regarding the possibility of cooperating with the St. Louis Hospital Pharmacists and the Nebraska Society in connection with sponsoring an institute at the Midwest Hospital Convention.

A special meeting of the Greater Kansas City Society was held on October 30 at St. Joseph Hospital. Mr. Paul Parker, President of the ASHP was the guest of honor. Mr. Parker spoke on our obligations as professional pharmacists and the need for raising standards in hospital pharmacy. He also discussed the proposed Formulary Service and the work being carried out by the A.Ph.A. and the ASHP through the Division of Hospital Pharmacy.

Greater New York Chapter

The first meeting of the Greater New York Chapter of the American Society of Hospital Pharmacists for 1956-57 was held at St. Catherine's Hospital, Brooklyn, N.Y., on October 17, 1956, at 2:30 P.M. The speaker was the Reverend Chaplain of the Hospital, Father O'Rourke. In a short talk he elaborated on a passage from Virgil's Aeneid: "Pharmacy is an inglorious, silent art." Then too, the pharmacist lacks the consolation derived from seeing the sick patient improve and, finally, get well under treatment.

During the business session the ballot envelopes were opened with the following results for new officers of the Greater New York Chapter: *President* Sister M. Jeanette, Mary Immaculate Hospital, Jamaica, N.Y.; *Vice-President* Sister M. Virginia, Mercy Hospital, Rockville Center, N.Y.; *Corresponding Secretary* Sister Maria Joseph, St. Joseph's Hospital, Far Rockaway,

N.Y.; *Recording Secretary* Sister M. Nicodema, St. Peter's Hospital, Brooklyn, N.Y.; and *Treasurer* Sister M. Angeline, St. Mary's Hospital, Brooklyn, N. Y.

New Jersey Society

Members of the New Jersey Society of Hospital Pharmacists met at the Rutgers College of Pharmacy in Newark on September 20. Features of the business meeting included reports on the 1956 pharmacy institutes. Sister Marion, S.C. of St. Elizabeth Hospital headed the Committee on Hospital Pharmacy Practice, and gave an excellent report on the institute sponsored by the Catholic Hospital Association in Milwaukee. Mr. Larry Pesa of St. Mary's Hospital, and Mr. Robert Calvo of Hackensack Hospital gave reports on the hospital pharmacy institute held at Austin, Texas. Mr. Angelus Bellino of Beth Israel Hospital, attended a course on radioisotopes given by the Philadelphia College of Pharmacy and Science, and gave a report on the highlights of the lectures. Mr. Eugene Von Stanley of Mercer Hospital, outlined the course on the manufacture of small volume parenterals as it was given by the Philadelphia College of Pharmacy and Science. Mr. Robert Calvo of Hackensack Hospital followed this with a presentation in color movies and an itemized summation of the manufacturing procedure, cost of operation, and relative merits of small volume parenteral manufacturing in a hospital. Dr. John Voight, head of the Extension Service of Rutgers College of Pharmacy, was the guest speaker of the evening. He pointed out the methods and efforts of this Branch of the College to keep in contact with the various branches of pharmacy, and to service its graduates.

The October meeting of the New Jersey Society of Hospital Pharmacists was held at the Hotel Plaza in Jersey City on the 18th. Dr. Morton J. Rodman of the Rutgers College of Pharmacy was the guest speaker of the evening, and gave an interesting address on "Economic Poisons." He distributed mimeograph sheets on the essential items that should be stocked in the Emergency Room, and the most practical reference books in use today. The role of the pharmacist in helping the community was discussed. Mr. Frank Megaro, Chairman of the Special Projects Committee on "A Pharmacist in Every Hospital," gave a report on the progress of this Committee. The resolution has thus far been whole heartedly approved by the Board of Pharmacy and the state pharmaceutical association. It now remains for a bill to be drafted and presented to the State Legislature. The nominating committee, under the Chairmanship of Mr. Keller, presented its slate of officers for the coming year. The meeting was preceded by a buffet supper sponsored by D. Kaltman and Co., Wholesale Druggists of Jersey City.

Above: Participants in the Meeting of the Nebraska Society, October 25 and 26. Left to right—Dan Moravec, Past President, George L. Phillips, Guest Speaker, Frances Rodgers, Program Chairman, and Garvin Muirhead, President. Below: Officers of the Nebraska Society. Left to right—Frank Franco, Secretary; Garvin Muirhead, President; and Lillian Dorsey, Treasurer.

Texas Society

The Executive Committee of the Texas Society of Hospital Pharmacists has recently voted to make a pledge to the A.Ph.A. Building Fund.

The Texas Society has also announced plans for the forthcoming Seminar which will be held on January 26 and 27 in Austin.

Houston Area Society

A "History of the Houston Area Society of Hospital Pharmacists," has recently been prepared by Miss Adela Schneider and Dr. Ruth Kroeger. The history will be submitted to the Committee on Historical Records and will become a part of the permanent SOCIETY Archives.

The Secretary of the Houston Area Society, Miss Dorothea Siler, has recently submitted detailed reports of regular monthly meetings of the group. Meetings have been scheduled at various hospitals and the Society has been particularly concerned with the various activities being carried out by the National Organization and cooperation with the current committees. Also, an outside speaker is usually brought in for each meeting.

The October meeting of the Houston Area Society was held at the M. D. Anderson Hospital. Following the business session, Dr. Hsu, of the M. D. Anderson Hospital spoke on "Tissue Culture Service to Pharmacology," and showed some interesting films to illustrate the subject.

Nebraska Society

New officers of the Nebraska Society of Hospital Pharmacists include *President* Garvin Muirhead;

Secretary Frank J. Franco; and *Treasurer* Lillian Dorsey.

Illinois Society

The various aspects of poisonings was the principal subject covered at the November 13 meeting of the Illinois Society of Hospital Pharmacists. Mr. Bernard Conley, Secretary of the Committee on Pesticides of the American Medical Association, was the principal speaker along with Mr. Charles Lev and Mr. Ed Hartshorn, both hospital pharmacists.

The meeting was held at the Hines Veterans Administration Hospital where the group was greeted by Mr. Harry Poole, Manager.

Another leader in hospital pharmacy who was present at the meeting was Mr. Joseph Oddis, a staff member of the Council on Professional Practice of the American Hospital Association. Mr. Oddis is a former hospital pharmacist and a past-president of the Western Pennsylvania Society.

Southern California Chapter

Eighty members and guests were present on October 26 for a special meeting which was called to welcome the National President, Mr. Paul Parker, to Los Angeles.

As the featured speaker for the evening, Mr. Parker chose to discuss "The Future of Professional Hospital Pharmacy as a Member of the Health Team." Briefly, he noted the increased importance of the hospital pharmacist and his relationship with hospital accreditation, the National Hospital Formulary Service and research projects now open to the pharmacists.

Chapter President, Miss Emily Alekna, presided at the meeting held at the local Upjohn Company Office.

Northern California Society

A Seminar for Hospital Pharmacists was conducted by the Association of Western Hospitals and sponsored by the Northern California Society of Hospital Pharmacists in Berkeley on October 13 and 14. Mr. Paul Parker, President of the ASHP, was present to represent the National Organization.

Among the principal papers presented during the two day meeting were the following:

"Education for Hospital Pharmacists," by Dr. Troy C. Daniels.

"New Philosophies for Hospital Pharmacy Internships," by Dr. Ivan Rowland.

"The Hospital Pharmacists' Role in the Handling of Radioisotopes," by Dr. Donald C. Brodie.

"Preparation of Sterile Ophthalmic Solutions," and "Practical Application," by Dr. Sidney Reigelman and Mr. Eric Owyang.

"Public Relations," by Professor Allen Zahn.

"Autonomic Drugs," by Dr. Frederick Meyers.

"Pharmacy Laws and How They Affect Hospital Pharmacists," by Floyd Heffron.

"The Pharmacist's Responsibility as Education Advisor—And Secretary of the Therapeutics Committee," by Charles G. Towne.

"The Pharmacist as Part of the Management Team," by Jerome M. Yalon.

Another highlight of activities in the Northern California Society was the One-Hundredth Meeting of the group which was celebrated with a dinner at the Sun Hung Heung Restaurant in San Francisco. Following the dinner the meeting was called to order by President Marie B. Kuck who discussed the organization of the Society and introduced the past-presidents including Jerome Yalon, Francis Spinelli, Chase Holaday, Charles Bertrand, and Claude Busick. Mr. Jack Heard and Mr. Alphonse Seubert who also served as past-presidents were unable to attend. A highlight of the dinner was the presentation of a large anniversary cake which was given by Pfizer Laboratories.

Western New York Society

Approximately seventy hospital pharmacists met on October 6 at the University of Buffalo to participate in a Hospital Pharmacy Seminar sponsored by Pfizer Laboratories in cooperation with the University of Buffalo School of Pharmacy and the Western New York Chapter of the American Society of Hospital Pharmacists. Hospital pharmacists came from as far east as Albany and as far west as Erie, Pennsylvania to participate in the Seminar.

The day long program which was enthusiastically received, proved to be informative and thought provoking. The morning session consisted of the following program:

Welcome by participating organizations:

Prof. Daniel Murray, Dean of the University of Buffalo School of Pharmacy.

Mr. Herbert Rieman, President, Western New York Branch ASHP.

Mr. Paul Parker, President, ASHP and Director of the Division of Hospital Pharmacy of the A.Ph.A. and of the ASHP.

"Application of State Pharmacy Laws and Regulation to Hospital Pharmacy," by Mr. Mearl Pritchard, Member of the New York State Board of Pharmacy.

"New Advances in Drug Therapy,"—Dr. Julian Ambrus, Senior Cancer Research Scientist, Roswell Park Memorial Institute and member of the U.B. Medical School Faculty.

"The Pharmaceutical Industry and Hospital Pharmacy,"—Mr. Charles W. Gill, Hospital Field Supervisor, Pfizer Laboratories.

"The Pharmacist's Responsibility as Secretary of the Therapeutics Committee,"—Paul Parker.

The guest speaker at the luncheon, Dr. Richard Heindel, Vice Chancellor, University of Buffalo Planning and Development, outlined future plans for the University of Buffalo and expressed the hope of offering more in the way of pharmaceutical extension service in the future.

A panel discussion in the afternoon covering several subjects of interest to hospital pharmacists such as pricing, salaries, parenteral solution manufacturing, etc. was ably moderated by Dr. A. Bertram Lemon, Dean Emeritus, University of Buffalo, School of Pharmacy. Members of the panel were: Dr. Fraser Mooney, Director, Buffalo General Hospital; Sister Mary Vera, Chief Pharmacist, Mercy Hospital, Buffalo; Dr. Clifton F. Lord, Jr., Assistant Professor of Pharmacy and Director Hospital Pharmacy Division, University of Buffalo School of Pharmacy and Mr. Charles Gill of Pfizer Laboratories. The program was concluded with a talk by Mr. Paul Parker entitled, "The Road Ahead for Hospital Pharmacy."

Dr. Clifton F. Lord, Jr., of the School of Pharmacy and Program Chairman for the Western New York Branch of the ASHP, acting as moderator for the Seminar, indicated that an attempt will be made to make this seminar-type program for hospital pharmacists an annual event.

Massachusetts Society

Members of the Massachusetts Society of Hospital Pharmacists met for a dinner meeting at the New England Deaconess Hospital in Boston on September 19. The meeting was called to order by President Schraub with an attendance of 38 members. Business discussed during the meeting included the availability of malpractice liability insurance, the possibility of the National Organization considering a group insurance plan, representation on national committees, and presentation of an annual award to a worthy hospital pharmacist in New England.

The program included an amusing talk by Dr. A. B. Krall of the New England Deaconess Hospital. His subject was, "Anti-diabetic Drugs."

The November 14 meeting of the Massachusetts Society of Hospital Pharmacists was held at the Children's Medical Center in Boston. During the business session President Schraub read the resignation of the Secretary-Treasurer, Miss Thelma Lezberg. Mr. James Durkee of the Children's Medical Center, was chosen Secretary-Treasurer to complete the unexpired term.

Mr. Joe Shibel reported on the successful seminar of the New England Council of Hospital Pharmacists which was held in Hartford, Conneticut on October 30 and 31.

Following the business session, Mr. John Curran, Associate Professor of Law at Boston College, spoke on "The Legal Responsibilities of Hospital Pharmacists and Legislative Development in the Regulation of Hospital Pharmacies."

Philadelphia Association

The Philadelphia Hospital Pharmacists' Association cooperated in sponsoring a one day Seminar in Philadelphia on November 8. Comprehensive coverage of a variety of subjects, ranging from "Effective Communications for the Hospital Pharmacist" to "New Concepts in the Preparation and Dispensing of Sterile Ophthalmic Solutions," drew over 200 hospital pharmacists and administrators to this first annual Hospital Pharmacy Seminar.

The one-day seminar, sponsored in cooperation with Pfizer Laboratories, The Philadelphia College of Pharmacy and Science, Temple University School of Pharmacy, the Hospital Council of Philadelphia, and the Philadelphia Hospital Association, provided hospital pharmacists from the Pennsylvania, New Jersey and Delaware areas an opportunity to learn of the most recent advances in techniques and theories particularly applicable to the specialized field of hospital pharmacy.

Participants in the Philadelphia Seminar: Left to right standing—Herbert L. Flack, Joseph V. D'Ambola, Paul Wilson, Dr. Linwood F. Tice, Dr. Joseph B. Sprowls, Robert Bogash and Arch Eglin. Left to right seated—Mrs. Gloria Francke, Norris George, Dr. Ivor Griffith, and Sister Mary Berenice.

Among the featured speakers were Sister Mary Berenice, Director of Pharmacy Service, St. Mary's Group of Hospitals, St. Louis, Mo.; Mr. Robert C. Bogash, Director of Pharmacy Service, Lenox Hill Hospital, New York City; Mr. Joseph V. D'Ambola, Director of Pharmacy Service, Hahnemann Medical College Hospital, Philadelphia; Dr. Joseph B. Sprowls, Dean, Temple University School of Pharmacy; Mr. Paul Wilson, Pfizer Laboratories, and Dr. Linwood F. Tice, Assistant Dean, Philadelphia College of Pharmacy and Science.

Mr. Herbert L. Flack, President of the Philadelphia Hospital Pharmacists' Association, expressed the satisfaction of the participating organizations at the good attendance, stating that it indicated an awareness by those present, of their continuing responsibility to the patient, the administrator, and the other members of the public health team.

Northeastern New York Society

The November 15 meeting of the Northeastern New York Society of Hospital Pharmacists was held at the St. Peter's Hospital in Albany. The business meeting started at 8:00 P.M. followed by reports from various committee chairmen. One of the projects for the coming year is revision of the Constitution of the local group. During the business session the Northeastern Society also voted to make a group contribution to the building fund of the A. Ph. A.

Rhode Island Society

The Rhode Island Society held the bimonthly meeting on Friday, November 16 at McKesson and Robbins auditorium in Hartford. The meeting was devoted almost entirely to business, including plans for the future programs and possible ways of interesting new members in the group. A special meeting was also called with regard to changes in the Constitution and By-Laws of the Rhode Island Society.

The group will meet on January 11 at the Veterans Administration Hospital in Hartford. The program will include a film and a speaker from the Schering Corporation.

Dade County Society

The Southeastern Florida Society of Hospital Pharmacists has recently voted to change the name of the organization to "Dade County Society of Hospital Pharmacists." The group recently held a joint meeting with the Miami branch of the American Pharmaceutical Association.

as the president sees it

PAUL PARKER

American Pharmaceutical Association, Washington, D. C.

I would like to encourage every member of the SOCIETY to begin making plans to attend our annual meeting in New York on April 28th, 29th and 30th. This is the one time each year when every hospital pharmacist has the opportunity to be personally concerned with and a part of the organized effort to better our professional specialty. The hospital pharmacists of New York City are making elaborate plans to help make the meeting a memorable occasion.

Attending the annual meeting can be of value in improved job performance. Both technical and general type papers are presented as a regular part of the program. You can become acquainted and compare notes with hospital pharmacists across the nation. Your attendance can be helpful to you, the SOCIETY, and the pharmaceutical profession through your association with practitioners of all segments of pharmacy.

At the annual meeting all our activities for the year are summarized in the form of reports from the officers and committees to serve as an implement for establishing policies to guide the future of our organization. The delegates from each of the 46 affiliated chapters may make recommendations in the establishment of these policies. New officers are installed, new committees are appointed, new assignments are made, and goals set to guide our progress during another year. An annual meeting might be compared to a New Year holiday. Goals are set and resolutions made. Never are all our high objectives completely achieved, nor our good intentions completely kept, but each annual convention marks tangible progress in hospital pharmacy.

Each year that you, as an individual, put off attending your first convention or each convention you miss, means one full year in which you may have not used the maximum opportunity to become an integral part of the professional activities of your SOCIETY.

Another item which I should like to call to your attention is the fine relationship between the A.S.H.P. and the American Hospital Association. This relationship was recently re-emphasized to me as I participated in a meeting of the Joint Committee of the A.S.H.P. and the A.H.A. It was a unique experience to sit for a day around the conference table with hospital administrators representing the A.H.A., each an authority in his field. It was interesting to observe the appreciation that these men had of hospital pharmacy problems. It was encouraging to note their recommendations to further our professional objectives through the close working relationship of our two associations.

For some time the Joint Committee has recommended the development of a manual on hospital pharmacy. The A.H.A. has obtained the services of Mr. Joseph Oddis, a hospital pharmacist, who will write this manual during the next year or two. Joe is sincerely dedicated to the highest interests of hospital pharmacy and he has achieved a high reputation for his ability as a hospital pharmacist and an organizational leader in his native city of Pittsburgh.

Hospital pharmacists may obtain personal membership in the American Hospital Association for $15.00 a year. Personal membership in that association brings *Hospitals,* the official journal of the A.H.A.; *Administrators Guide,* a very useful compilation of facts and statistics about hospitals and their operation, and *This Month,* a newsletter to keep you posted on what's going on and what's likely to be going on in hospital affairs. Membership also gives you the privilege of using the resources of the A.H.A.'s library, one of the finest of its kind in the country, obtaining their manuals and publications, and obtaining the advise of their staff specialists. Since your career is in the hospital field, as well as the pharmacy profession, I would recommend your personal membership in this fine organization.

Paul F. Parker

NEWS

Executive Committee Meets

The Executive Committee of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS met at the Dupont Plaza Hotel in Washington, D. C. on November 12 and 13. Members of the Committee attending included: Paul Parker, Milton Skolaut, Gloria Niemeyer Francke, Sister Mary Berenice, Robert Bogash, Clifton Latiolais, Grover C. Bowles, Claude Busick, and Leo F. Godley. Others participating in various parts of the meeting included Don Francke, Editor of THE BULLETIN of the ASHP, Allen V. R. Beck, a Past-President of the SOCIETY and Chairman of the Committee on Constitution and By-Laws, William Heller, Chairman of the Committee on Pharmacy and Pharmaceuticals, and Dr. Robert P. Fischelis, Secretary of the American Pharmaceutical Association. Also present for the sessions was Sister Mary Cecilia, companion to Sister Berenice. Dr. George Archambault, a Past-President of the SOCIETY met with the group for part of an evening session to discuss several ASHP activities with which he is concerned at the present time.

The Committee met for two days during which time detailed reports on Committee activities to date were presented along with recommendations for action. Of particular note were the discussions on the work of the Committee on Pharmacy and Pharmaceuticals and the progress being made on the *American Hospital Formulary Service*; the work of the Committee on Research and Development and authorization of the Executive Committee to present grants to carry out specific research in the field of hospital pharmacy; and plans for the 1957 Annual Meeting.

Among the actions taken which are of particular significance to the members of the SOCIETY are the following:

—Approved the San Diego Society of Hospital Pharmacists for affiliation with the ASHP.

—Reconsidered the status of membership in affiliated chapters and voted to continue to insist that all members of affiliated chapters of the ASHP be members of the national organizations.

—Approved the work of the Committee on Research and Development and agreed to the recommendation that two grants be made for research in hospital pharmacy. These include: (1) A grant to John W. Webb and Anthony Ciampo to study "The Sterilization of Ophthalmic Ointments by Using a Van De Graaf Electron Accelerator;" and (2) A grant to Don E. Francke to prepare "Selected Annotated Bibliography on Hospital Pharmacy."

—Approved signing a contract for printing the *American Hospital Formulary Service*.

—Recommended that the Committee on Minimum Standards continue work on the preparation of a Syllabus for a Course in Hospital Pharmacy.

—Approved plans for the 1957 annual meeting.

—Agreed to be a sponsoring organization for the Pan-American Congress on Pharmacy which is to be held in Washington, D. C. in November 1957.

—Authorized the Editor of THE BULLETIN to proceed with activities to launch publication of a second journal in the field of hospital pharmacy. It was agreed that this publication should be directed to all hospital administrators.

—Approved changing the name of the Committee on Economic and Household Poisons to "Committee on Economic Poisons."

During the meeting of the Executive Committee, the members also heard a detailed report on the work which is being carried out in the affiliated chapters. This was presented by president Paul Parker, who has recently visited a great number of the chapters in the west and has had contacts with many members of the SOCIETY.

Joint A.H.A.—ASHP Committee Meets

The Joint Committee of the American Hospital Association and the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS met at the Hotel Statler in Washington on December 10. Representatives of the American Hospital Association present included Dr. Robert R. Cadmus, North Carolina Memorial Hospital, Chapel Hill; Dr. August R. Groeschel, The New York Hospital, New York City; Mr. Joe Vance, South Highlands Infirmary, Birmingham, Alabama; and *ex officio* members Dr. Leroy Bates, who was present in the absence of Dr. Sarah Hardwicke, Secretary of the A.H.A.'s Council on Professional Practice; and Mr. Joseph A. Oddis, a staff pharmacist at the American Hospital Association. Mr. John Zugich, University Hospital, Ann Arbor, Michigan, another representative of the A.H.A., was unable to be present. Representatives of the SOCIETY included Dr. George F. Archambault, Washington, D. C.; Dr. Don E. Francke, Ann Arbor, Michigan; Mr. Walter M. Frazier, Springfield, Ohio; and Paul F. Parker, Washington, D. C. Mrs. Gloria Francke was present as an *ex officio* member of the Committee.

A wide variety of subjects affecting pharmacy practice in hospitals was discussed. Of considerable importance were further proposals to the Joint Commission on Accreditation for guides to be used in the inspections of hospital pharmaceutical services; a proposed revision of the 1937 A.H.A. Report on Hospital Pharmacy; and the use of tax free alcohol in hospitals. Also, a preliminary draft of the proposed Hospital Pharmacy Manual was presented by Mr. Oddis and plans were outlined for proceeding with actual writing of the manual.

A.A.A.S. Meets in New York City

Hospital pharmacists participated in the Pharmacy Section Np of the 1956 Convention of the American Association for the Advancement of Science, held at the Hotel Statler in New York City on December 26-29. The Hospital Pharmacy Sessions, presented under the direction of Dr. George F. Archambault, were held on Saturday, December 29. An outstanding meeting was reported with hospital pharmacists from the New Jersey, New York and Pennsylvania areas participating. Affiliated chapters represented included the Greater New York Chapter of the ASHP, the Southeastern New York State Chapter of the ASHP, the New Jersey Society of Hospital Pharmacists, the Connecticut Society of Hospital Pharmacists, and the Philadelphia Hospital Pharmacists' Association. President Paul Parker represented the national organization. Papers presented at the Hospital Pharmacy Sessions included the following:

"State Supervision and Control Over Drug Distribution," by Leavitt C. Parsons, Publisher, *The Apothecary,* Boston, Mass.

"Concluding Report on Significant Cost Data Pertaining to the Administration of Certain Injectables Using the Conventional Syringe and Needle Technique Versus the Closed System Sterile Disposable Units," by James A. Hunter, M.D., Medical Director, Medical Officer in Charge, U. S. Public Health Service Hospital, Detroit, Michigan; and David Zaugg, M.D., Medical Director, Medical Officer in Charge, U. S. Public Health Service Hospital, Baltimore, Md. and others.

"The Law Imposed Responsibilities on the Hospital Pharmacist," by Louis E. Kazin, Associate Editor, *Drug Topics* and *Drug Trade News,* New York City, N. Y.

"The Need for a More Meaningful Professional Degree for Hospital Pharmacists," by Don Francke, D. Sc., Editor THE BULLETIN OF THE AMERICAN SOCIETY OF HOSPITAL PHARMACISTS, Ann Arbor, Mich.

"The Value of Scientific Management of Drug and Pharmaceutical Resources in Private and Voluntary Hospitals and Clinics," by Seymour B. Jeffries, Member of Faculty, Brooklyn College of Pharmacy, Brooklyn, N. Y.

"The Current Status of (a) the National Audit of Pharmaceutical Service in Hospitals under U. S. Public Health Service Grant, (b) Internship Accreditation and Number of Pharmacy Internships in the United States, and (c) the American Hospital Formulary," by Clifton J. Latiolais, Assistant Director, Audit of Pharmaceutical Service in Hospitals, Ann Arbor, Mich.

"Intradermal Skin Testing Materials for the Diagnosis of Disease," by Edward Croumey, Chief Pharmacist, Mary Fletcher Hospital, Burlington, Vt.

"A Narcotic-Hypnotic Hospitalwise Control System Applicable to Small and Large Hospitals," by Arthur W. Dodds, Ph.C., Director, Pharmaceutical Service, U.S. Public Health Service Hospital, Staten Island, New York, also Training Officer, U. S. Public Health Service Pharmacy Internship Program and George F. Archambault, D. Sc., LL.B., Chief, Pharmacy Branch, Division of Hospitals, U.S. Public Health Service, Department of Health, Education and Welfare, Washington, D. C.

A panel discussion of the papers followed the presentation with the following participants: Paul Parker, Newell Stewart, Fred Lascoff, R. Zimmerman, Joseph Oddis, Robert Bogash, Herbert Flack, and E. E. Leuallen.

Luncheon, entertainment and dinner were sponsored during the day by Squibb, Wyeth and Pfizer.

Maryland—D.C.—Delaware Association

Among the many interesting section meetings of the 16th Annual Conference of the Maryland-District of Columbia-Delaware Hospital Association held at the Shorham Hotel, Washington, D. C., on October 31, November 1 and 2, 1956, was the Pharmacy Section Meeting sponsored by the Maryland Association of Hospital Pharmacists.

In keeping with the general theme of the Conference, "Management For Progress," a stimulating and informative presentation of a Pharmacy-Operated Central Supply Service was offered by a

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group of panelists from the Clinical Center of the National Institutes of Health, Bethesda, Maryland, including a Medical Director, Chief Pharmacist, Administrator, Chief Nurse, and Operating Room Supervisor.

Panelists included the Moderator, Stuart M. Sessoms, M.D., Assistant Director; Mr. Milton W. Skolaut, Chief, Pharmacy Department; Mr. Philip P. Simon, Administrative Officer; Miss Ruth L. Johnson, Chief, Nursing Department; and Miss Janet L. Fitzwater, Chief, Surgical Nursing Service. All are commissioned officers of the United States Public Health Service stationed at the Clinical Center, National Institutes of Health, Department of Health, Education, and Welfare, Bethesda, Maryland.

After each of the panelists discussed this relatively new area of hospital pharmacy practice from the standpoint of his own position, questions from the nearly 100 hospital pharmacists and allied personnel in attendance at the meeting were directed to the panel member most qualified to comment on the particular problems posed by the questions.

At the conclusion of the discussion period, the formal installation of the officers of the Maryland Association of Hospital Pharmacists for the coming year took place. They are: President—Mr. William H. Briner, Clinical Center, National Institutes of Health, Bethesda, Maryland; Vice-President—Miss Mary DiGristine, Lutheran Hospital of Maryland, Inc., Baltimore, Maryland; Secretary—Miss Mary W. Connelly, Bon Secours Hospital, Baltimore, Maryland; and Treasurer—Mr. Dudley A. Demarest, Frederick Memorial Hospital, Frederick, Maryland.

The program for the Section Meeting was arranged by Dr. John A. Scigliano, immediate Past-President of the Maryland Association of Hospital Pharmacists.

New England Council of Hospital Pharmacists

The New England Council of Hospital Pharmacists held its Third Annual Seminar on October 30 and 31 at the Hotel Statler, Hartford, Connecticut. More than 60 hospital pharmacists from throughout the New England area were in attendance.

Highlights of the Seminar included talks by Mr. Stuart Knox of the Connecticut Hospital Association, Dr. Richard Thoms of the University of Connecticut, College of Pharmacy, Dr. J. Martin of the Anesthesiology Department, Saint Francis Hospital, Hartford, Mr. W. Cairns of Eli Lilly Company, Mr. T. J. Walker of the

Bureau of Narcotics and Mr. Leo Godley, President-Elect of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS.

The Seminar Committee included members of the hospital pharmacy organizations in the New England States. This year's President of the Seminar was Mr. Edmund Singer of Norwalk Hospital, Norwalk, Connecticut and the Secretary-Treasurer was Mrs. Ruth Summers of Charlotte Hungerford Hospital, Torrington, Connecticut. The Seminar elected Mr. Edward Gilberti of Rhode Island State Hospitals and Institutions as President for the coming year. The Secretary-Treasurer is Mr. Victor Canaipi of Wallum Lake State Hospital, Rhode Island.

Dr. Fischelis Elected 1956 Man of the Year

Robert P. Fischelis, Secretary of the American Pharmaceutical Association, has been elected as the retail drug field's Man of the Year 1956.

The Man of the Year award was established by *American Druggist,* fortnightly magazine of the drug trade, to honor the man who, each year, makes the most constructive contribution to the welfare of the retail drug field this year.

The selection is made by a panel of drug industry leaders, including the presidents and secretaries of all national, state, and local pharmaceutical associations and boards of pharmacy, the deans of all accredited colleges of pharmacy, and the editors of all national, state, and sectional drug publications.

Dr. Fischelis was named Man of the Year because, during 1956, he played a leading role in crystallizing and presenting the views of those in the drug field who see dangers to public health in the procedure whereby a drug which has been limited to sale on prescription only is released by the government for sale without a prescription. He represents many pharmacists who believe that potent drugs which are transferred from prescription-only to over-the-counter status may be misused by purchasers who do not fully understand or heed the cautions given on the labels.

Dr. Fischelis is a 65-year-old native of Philadelphia. He was at one time dean of the New Jersey College of Pharmacy and later, for 16 years, secretary of the New Jersey Board of Pharmacy. During World War II, he organized and headed the Drugs, Chemicals & Health Supplies division of the War Production Board. He has been secretary of the American Pharmaceutical Association since 1945.

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A.A.C.P. Sponsors Teachers Seminar

The American Association of Colleges of Pharmacy 1957 Teachers Seminar will be held at the University of Washington, College of Pharmacy, Seattle, Washington during the week of July 14. The special Seminar Committee consists of: Dean Jack E. Orr, University of Washington College of Pharmacy, Chairman; Dr. James M. Dille, University of Washington School of Medicine; Dr. Ewart Swinyard, University of Utah College of Pharmacy; Dr. George L. Webster, University of Illinois College of Pharmacy; and Dean Louis C. Zopf, State University of Iowa College of Pharmacy.

Dr. Nathan A. Hall, University of Washington College of Pharmacy and Dr. Theodore C. West, University of Washington School of Medicine will serve in an advisory capacity to the special committee. The Seminar this year will be devoted to the subject of pharmacology. Detailed information will soon be available regarding the program. Information concerning housing facilities and recreational opportunities will be forwarded to all Colleges of Pharmacy by Chairman Orr in the very near future.

Don Francke presents A.Ph.A. and ASHP Membership Certificates to Baxter Sales Force. Left to right: Charles Dolan, Raymond D. Hetterick, Don E. Francke, and George Marks.

Baxter Sales Force Joins ASHP En Masse

Fifty-eight members of the sales force of Baxter Laboratories, Inc. were presented joint memberships in the American Pharmaceutical Association and the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS at a meeting in Chicago on December 7th.

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Lakewood Hospital Morgan City, Louisiana	General Hospital Annapolis, Maryland
Dixie Hospital Hampton, Virginia	Ayden Clinic Ayden, North Caroli
N. E. Baptist Hospital Boston, Mass.	Liberty Co. Hospital Chester, Montana
Calais Regional Hospital Calais, Maine	Blue Hill Hospital Blue Hill, Maine
St. Elizabeth Hospital Utica, New York	Alexandria Hospital Alexandria, Virginia
Greenwood Co. Hospital Eureka, Kansas	Mayview State Hosp Mayview, Pa.
Hart Co. Med. Center Hartwell, Georgia	Ill. Central Hospital Chicago, Illinois

This was the occasion of the 25th anniversary of the company and members of the sales force from throughout the country participated. Certificates of membership were presented by Dr. Don E. Francke, a past president of both the A.Ph.A. and the ASHP. On presenting the memberships, Dr. Francke complimented Baxter Laboratories and their sales promotion manager, Mr. Charles F. Dolan, for the interest shown in the national pharmaceutical organizations and pointed out the need for cooperation between industry and hospital pharmacy.

Member of Policy Committee Changes Post

Sister M. Stephanina, O.S.F., who has served as Administrator of St. Francis Hospital, Evanston, Illinois, has been elected assistant to the Mother Provincial. She has been a member of the Policy Committee of the Division of Hospital Pharmacy of the American Pharmaceutical Association and the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS since 1953. Sister Stephanina is now assigned to the motherhouse of the Community of St. Francis in Mishawaka, Indiana.

Parker Visits VA Hospital, Los Angeles

Mr. Paul Parker, Director, Division of Hospital Pharmacy of the American Pharmaceutical Association, reviewed the residents' training program for pharmacists at Veterans Administration Center, Los Angeles, California, on October 26, 1956.

Mr. Parker's visit was made for the purpose of evaluating the program which is being considered for accreditation by the Division of Hospital Pharmacy of the American Pharmaceutical Association and the AMERICAN SOCIETY OF HOSPITAL PARMACISTS.

Various officials of the Center were interviewed during Mr. Parker's inspection, and extensive discussions were held with Mr. Charles Towne, Chief of Pharmacy Service, and Mr. Chester Bazel, Chief Pharmacist of the Teaching Section of the VA Center. A further insight into the effectiveness of the teaching program was gained through interview of the pharmacy residents. This included the three new pharmacy residents who reported in September of this year to commence their two-year training at this Center. They are: Mr. James Elieff (B.S., 1952, Purdue University), from

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Mr. Parker interviews Residents at Los Angeles VA Hospital. Left to right—A. Warren, J. Elieff, Paul Parker, D. Friedmann, and C. Gilliam.

Indiana; Mr. Donald Friedmann (B.S., 1953, Temple University), from Pennsylvania; and Mr. Calvin Gilliam (B.S., 1956, Xavier University, New Orleans), from Louisiana. All residents are currently registered pharmacists and are working toward their Master of Science degree in hospital pharmacy at the University of Southern California. A total of six residents have completed this four-year-old program.

Lakeside Film Available

An interesting color film designed to inform the lay public of the research behind the prescription price is proving equally useful as a teaching aid in the nation's pharmacy colleges The film, "The Constant Search" was produced by Lakeside Laboratories.

In the film the company was not squeamish about the price of a prescription, according to Wyman Guin, vice-president in charge of advertising. "This scientific documentary explains what is behind that price," Mr. Guin said, "in the hope that the prescription price will ultimately speak for itself."

The company recently made the film available to all pharmacy colleges, he said. Lakeside hopes that professors might find it a useful tool in helping to train future pharmacists who will be confronted by the public relations problem of prescription prices.

Shortly after the film was offered to the pharmacy colleges more than 25 across the country accepted and most of them have already shown it to the students, Mr. Guin disclosed.

Mr. Guin said the company hoped the film will continue to play a role in the over-all program both of manufacturing and professional pharmacy to inform the public how relatively inexpensive prescriptions are compared with the general cost of living. He referred specifically to the literature of the National Pharmaceutical Council, distributed to the public through pharmacies, and the program of the Health News Institute.

NEW MEMBERS

JANUARY 1, 1957

The following ASHP members sponsored the New Members listed in this issue of THE BULLETIN. *The officers of the* SOCIETY *and the Committee on Membership and Organization appreciate the efforts of the individuals who have encouraged New Members to join the national organizations. Sponsors will be listed along with the New Members in each issue of* THE BULLETIN.

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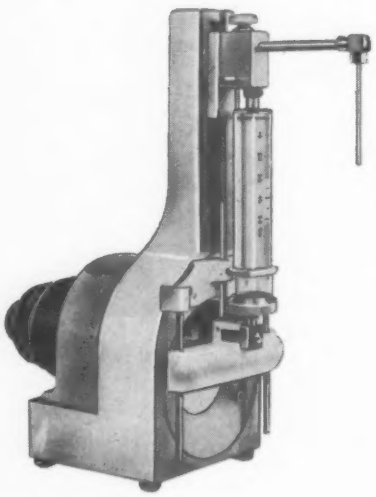

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Third Supplement

COMPREHENSIVE BIBLIOGRAPHY ON HOSPITAL PHARMACY

including publications to January 1957

compiled by

William Heller and Gloria Francke

THE BULLETIN American Society of Hospital Pharmacists

Vol 14 No 1 January-February 1957

published as a service

to those

interested in Hospital Pharmacy --

practitioners, students, educators, et al --

by

The BULLETIN

of the

American Society of Hospital Pharmacists

This Third Supplement to the *Comprehensive Bibliography on Hospital Pharmacy* is a continuation of the original Bibliography and Supplements published in the January-February (1951, 1953, and 1955) issues of THE BULLETIN OF THE AMERICAN SOCIETY OF HOSPITAL PHARMACISTS. With few exceptions, the references included in this Third Supplement are taken from journals appearing in 1955 and 1956.

This compilation of references to the literature in hospital pharmacy is intended to serve practitioners, students, and teachers in this specialty. With each new Supplement, additional journals have been covered and new subject headings added to encompass the new fields of endeavor related to hospital pharmacy. The growing importance of hospital pharmacy is evidenced by the increasing volume of literature being published.

Preface to Third Supplement

In compiling the Bibliography, principal subject headings have been chosen and arranged in a manner most convenient for use. No attempt has been made to include an index, but headings have been chosen to cover broad subjects. Occasional duplications have been made in order that one using a list of references on a particular subject will have the advantage of finding each subject and each entry self-contained without referring elsewhere. Subject headings are arranged alphabetically with references arranged chronologically, the most recent articles appearing first under each heading. Articles appearing within each year are separated by a line. The names in the author index, arranged alphabetically without distinction as to sole or joint authorship, are followed by numbers which refer to the reference number of each article written by a particular author. Page numbers are not referred to in the author index.

This work is published by THE BULLETIN OF THE AMERICAN SOCIETY OF HOSPITAL PHARMACISTS as a service to those interested in hospital pharmacy. The SOCIETY, at its 1952 Annual Meeting, endorsed this activity and urged that provision be made for issuance of regular supplements.

Publication of this Third Supplement to the *Comprehensive Bibliography on Hospital Pharmacy* has again been made possible through the efforts of William Heller, Ph.D., who is responsible for compiling the major part of the work. Dr. Heller is Chief of Pharmacy Service at the University of Arkansas Medical Center, Little Rock, Arkansas.

Gloria Francke

Ann Arbor, Michigan
January, 1957

Principal Journals Cited in Bibliography with ABBREVIATIONS

American Journal of Pharmaceutical Education—
Am. J. Pharm. Ed.

American Journal of Pharmacy—
Am. J. Pharm.

American Professional Pharmacist—
Am. Profess. Pharmacist

The Bulletin of the American Society of Hospital Pharmacists—
Bull. Am. Soc. Hosp. Pharm.

Bulletin De La Federation Internationale Pharmaceutique—
Bull. F. I. P.

Bulletin of the National Association of Boards of Pharmacy—
N.A.B.P. Bull.

Hospital Management—
Hosp. Management

The Hospital Pharmacist (Canada)—
Hosp. Pharm.

Hospital Progress—
Hosp. Progress

Hospitals—
Hospitals

The Journal of the American Medical Association—
J. Am. Med. Assoc.

Journal of the American Pharmaceutical Association,
Practical Pharmacy Edition—
J. Am. Pharm. Assoc., Pract. Pharm. Ed.

The Modern Hospital—
Modern Hosp.

The Pharmaceutical Journal (London)—
Pharm. J.

Southern Hospitals—
South. Hosp.

NOTE: Arrangement of individual references is according to the following style:

Author: Title of Article, Name of Periodical (in italics), volume number: page number (month) year.

Numbers of the periodicals have not been included since the month is always listed. Journals which are referred to most frequently are listed above, along with the abbreviations as used throughout the bibliography.

Subject Headings

Third Supplement to Bibliography on Hospital Pharmacy

ADMINISTRATION (Reference 1 through 118)

General Organization and Administration

Cost of Medications
Pricing, Drug Charges, etc.

Dispensing, Labeling, and Storage

Personnel and Salaries

Policy

Purchasing

Records and Reports

Stock Control
Ward Stocks, Inventory, After Hours, etc.

ALCOHOL (119-124)

AMERICAN HOSPITAL ASSOCIATION (125-130)
See also Institutes

AMERICAN PHARMACEUTICAL ASSOCIATION, and AMERICAN SOCIETY OF HOSPITAL PHARMACISTS (131-224)
Includes Division of Hospital Pharmacy, Audit of Pharmaceutical Service in Hospitals and references to ASHP Affiliates

CATHOLIC HOSPITAL ASSOCIATION
See Institutes

CLINIC PHARMACIES (225-236)

DEPARTMENTS, descriptions of (237-249)
Includes hospital pharmacies in specialized institutions

DETAIL MEN (250-262)

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EQUIPMENT and FIXTURES (311-333)
Includes equipment used in manufacture of parenteral solutions

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EXHIBITS (334-361)

FLOOR PLANS and PLANNING (362-370)

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Army

Navy

Public Health Service

Veterans Administration

HISTORY (446-461)

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Includes Refresher Courses, Seminars and Workshops

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INVESTIGATIONAL DRUGS
See Pharmacy and Therapeutics Committee

LAWS and REGULATIONS (567-581)

LIBRARY and REFERENCE (582-612)

MANUFACTURING or BULK COMPOUNDING (613-628)
Includes special procedures used in hospital pharmacy

MINIMUM STANDARDS
See Standards and Standardization

NARCOTICS (629-643)

OUTPATIENT DEPARTMENT (644-650)

PARENTERAL SOLUTIONS (651-698)
Includes Central Supply

PHARMACY AND THERAPEUTICS COMMITTEE (699-750)
Includes Formularies and ASHP Committee on Pharmacy and Pharmaceuticals

POISONS, POISONINGS
See Public Health and Medical Care

PROFESSIONAL RELATIONS (751-771)
Includes Ethics

PUBLIC HEALTH AND MEDICAL CARE (772-781)
Includes Health Insurance, Poisons . . .)

PUBLIC RELATIONS (782-801)

RADIOISOTOPES (802-814)

RESEARCH (815-843)

SMALL HOSPITALS (844-887)

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